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VOL. III JANUARY, 1908 No. 1

A COMPARATIVE STUDY OF TSUTSUGAMUSHI DISEASE AND SPOTTED OR TICK FEVER OF MONTANA.

By P. M. ASHBURN [1] and CHARLES F. CRAIG.[1]

I. SYNONYMY.

Tsutsugamushi disease; Japanese river fever; flood fever; island fever; *kedani* disease; *aka mushi* disease; *shima mushi* disease; *yochubio; shashitsu.*

Mushi is a Japanese word meaning bug, and the compounds ending with it all relate to the etiology of the disease. *Tsutsugamushi* is the term employed by most Japanese people and professional men and, as it has the prestige derived from ancient and specific usage, it will be employed in this paper.

[1] Captain and assistant surgeon, United States Army, and first lieutenant and assistant surgeon, United States Army, constituting the United States Army Board for the Study of Tropical Diseases, as they occur in the Philippine Islands.

Spotted fever of Montana; Rocky Mountain fever; tick fever; *Pyroplasmosis hominis* (Wilson and Chowing); tick fever of the Rocky Mountains; Rocky Mountain spotted fever.

As so-called spotted fever has been described as occurring in various districts of the Rocky Mountain region, and as it has not been determined that the same infection is identical in all those parts, the term *spotted or tick fever of Montana* will be used in this paper, the disease referred to being that occurring in western Montana, particularly in the Bitter Root Valley, in Missoula and Ravalli Counties.

II. INTRODUCTION.

For many years *kedani* or *tsutsugamushi* disease has been an annual subject of the most active and painstaking investigation on the part of Japanese physicians and the Japanese Government.

One of the leading investigators of late years is Dr. M. Miyajima of the Institute for Researches of Infectious Diseases, of Tokyo. Dr. Miyajima had read of the work of Wilson and Chowning, Anderson, Stiles and others on the study of "spotted" or "tick fever" in Montana and as he had found so many points of similarity in the two diseases, he thought it quite possible that they were the same. Consequently, when he came to Manila as a representative of his Government to the Philippine Islands Medical Association, he was desirous that we should visit Japan at the proper season and determine, if possible, whether or not such is the case. Thanks to the representations of Dr. Miyajima and the liberal view taken of the matter by Major-General Leonard Wood, the Acting Surgeon-General and the War Department, we were ordered to Japan; and this report is based on the observations concerning *tsutsugamushi* disease made on that trip and those of one us (Ashburn) in 1904 and 1905 on the cases of spotted fever occurring during those years in the Bitter Root Valley in Montana.

The specific point we were to endeavor to determine, and which we think we have determined, was the question of the identity or nonidentity of the two diseases and the greater amount of emphasis will be laid on that point in this report.

However, as both diseases are so closely restricted in their locality, and so are necessarily unknown to the very great majority of medical men, a brief account of each will be given and an effort will be made to place them side by side, so that the resemblances and differences may be brought out more strikingly. The descriptions to be given are based on personal observations of some twenty-two cases of "spotted fever" and seven cases of *tsutsugamushi* disease, as well as on the writings of others who have studied one disease or the other more carefully than we could.

Both infections are still subjects of earnest and careful investigation by

expert workers, and it is therefore unnecessary, and it would be futile, in a paper of this kind, to attempt the thorough consideration of them which they deserve and will receive later.

III. HISTORY OF THE TWO DISEASES.

According to Tanaka the name *tsutsugamushi* has been known since the earliest historical times, while the designation *shashitsu* occurs in Chinese writings more than a thousand years old. A quotation from one of these indicates that at the time the disease was recognized as a distinct affection and was ascribed to the bite of a mite, which occurred in summer time in certain districts which had been flooded by the spring rains. The bite was described and the statement made that after three days a high fever developed and a pustule appeared at the site of the injury. It was also recognized that only certain regions of the country harbored the infection and that the disease only appeared in persons entering them.

Tsutsugamushi was brought to the attention of the Western World by Palm in 1878 and by Bälz in 1879, and since that time it has been the subject of much painstaking work by Japanese medical men. Numerous articles have appeared in Japanese journals and a certain number of European ones; many microörganisms, including cocci, bacilli and protozoa, have been described as the cause of the disease, and several investigators are working at the present time, each with what he considers to be the causative factor. It can not be said that any one of these workers has as yet established his claim. Three hypotheses at present divide those actively engaged in the study of the disease and rule the work of investigation:

1. That the disease is caused by a bacterium, a belief favored by the workers of the Institute for Infectious Diseases.

2. That it is a protozoäl infection. Professor Ogata is the leading exponent of this idea.

3. Tanaka thinks it is due to a toxin contained in the body of the red mite.

Spotted fever of Montana has been recognized for only a few years, twenty-five at the most, while the literature relating to it has practically all been written since 1902. Wilson and Chowning in 1902 published their first account of the fever and gave their ideas as to its cause and the method of its transmission in a preliminary report to the Montana State board of health, which appeared in the Journal of the American Medical Association. It is true that Major Wood, in 1896, and Maxey in 1899 had reported a similar, or the same disease in Idaho, but the form occurring in the latter territory presents such points of difference, particularly in regard to mortality, that it is not considered in this paper.

The disease, since the work of Wilson and Chowning in 1902, has each year been the subject of careful investigation and report, and the prospects now are that its etiology will soon be well understood.

The total number of cases occurring each year is small and this fact, considered in connection with the further ones that the disease is encountered in such a limited and relatively isolated region and has been known for so short a time, makes it remarkable that the present knowledge concerning it should be as great as it is.

IV. ETIOLOGY.

Tsutsugamushi disease occurs along certain limited parts of the banks of a few rivers on the west coast of the main island of Nippon, being limited to Echigo and Akita Provinces. The distribution of the infected areas is irregular and, up to the present time, unexplainable. They are all subject to submergence by floods which occur in June, but not all flooded districts are infected, nor does the relative location of an infected district, up or down stream, seem to influence a noninfected one. The floods usually occur in June and last but a few days. Immediately after their subsidence the infective regions are not dangerous, but after a few weeks or a month and synchronously with the appearance of the *akamushi* or red mite, they become so, and any person entering them takes a considerable risk of contracting the disease. Consequently, these regions are avoided at this time by all whose poverty does not drive them there to work. As a general rule no right of ownership is exercised over such land and the very poor do, therefore, cultivate hemp on it in some places and in other parts visit it to gather mulberry leaves to feed silkworms. In either case they are apt to be bitten by red mites and it is customary for them to search carefully for their bites after leaving the places where they are encountered. However, the mites are so small as to be very difficult of detection and if the bite does not cause pain, it is frequently overlooked. Not all mites are infective and many bites therefore cause no trouble. However, a certain proportion of them do, the point bitten becoming an eschar and later an ulcer. The neighboring lymphatic glands become enlarged and painful and an attack of fever succeeds.

It is the experience of practically all who have carefully studied the disease, and they are numerous, that *every* case of it is preceded by the bite of a mite, and in the great majority of instances this is located by an examination of the region drained by the lymphatic glands, which first become enlarged and tender. So far as could be learned in Japan, Bälz's contention that such is not the case has not received support, and later investigators agree that the above method is the sole means of infection. The mite in question is the larval form of a *Trombidium*, species unknown. The larva bears a great resemblance to that of *Leptus autumnalis*. It is so small as to be almost invisible to the naked eye, it is

bright red or orange in color and is found on land that has been submerged by flood. Here it is best collected by tying a monkey out over night or by catching the field mice (*Arvicola hatanedzumi* Sasaki) occurring in such regions. The insects collect in groups on or about the eyelids of the monkey, while they are always found attached in large numbers to the inner surfaces of the ears of the mice. Mites resembling these in size and color occur in many parts of Japan, but they do not attack persons. The *akamushi* of other than infected regions do not transmit disease.

Several supposed causative organisms have been described for the infection, the latest and probably the one calculated to excite most interest being Ogata's plasmodium. None of these alleged discoveries has been confirmed, and judging from what we heard and such blood examinations as we could make in Japan, it appears that Ogata's plasmodium does not exist. The causative organism is as yet unknown.

Spotted or tick fever of Montana, as known by Wilson and Chowning, Anderson, Stiles, Ricketts and Ashburn, also occurs in very strictly limited areas, particularly in a strip of country about 4 to 10 miles wide and 50 miles long, lying on the west side of the Bitter Root River and the eastern side of the Bitter Root Mountains and partly on the slopes of the latter. The country in question has a considerable fall of snow which remains on the mountains until mid June and on the highest peaks for two or three weeks longer. The Bitter Root River is largely fed from this snow and, as it begins to melt in March and continues to do so with increasing rapidity until most of it has disappeared, the stream is in a state of freshet during this time and does not again reach "low water" until July. During the same period ticks (*Dermacenter occidentalis*), which before and after these freshets are infrequently seen, appear in great numbers, particularly in the forests, thickets and uncultivated regions, and they are very apt to get on any person or animal going into such parts. Cases of "spotted" or "tick fever" likewise, and as rule, appear during the same period, and in almost all instances of infection a history of a recent visit to, or residence in, the infected district, and in many cases an account of tick bites received there, is given. Wilson and Chowning identified the tick as the carrier of the disease as early as 1902. Ashburn, after a study of all the cases occurring in 1904 and most of those in 1905, came to the conclusion that a considerable proportion of these cases gave neither history nor signs of tick bite and, for that and other reasons which it is not necessary to detail here, agreed with Stiles that the tick was not concerned in transmitting the disease. However, the more recent and very excellent work of Ricketts and of King, and their apparent success in transmitting the infection to monkeys and guinea pigs by means of the tick, seem to indicate that Wilson and Chowning were right in their belief as to the method of transmission. It may therefore be said that the disease is

introduced by the bite of *D. occidentalis.* The location of the bite can not always be determined, possibly because the first symptoms of the fever do not indicate its position as is the case with *tsutsugamushi* disease. Certainly, an ulcer and lymphadenitis do not always follow. Ricketts's recent observation that nymphal ticks may transmit the disease and his suggestion that larvæ may do so, possibly accounts for the absence of a history of tick bite in some cases; as the lesion resulting from the bite of larvæ may be so insignificant as possibly to leave no trace after a few hours or a day and the larva itself may be overlooked. The majority of persons in the infected regions carefully watch and examine themselves for tick bites, and it is improbably that the bite of the adult tick is often overlooked. In nearly all cases the disease is contracted on the hill sides or "bench," high above the river, and some persons long resident in the region say that the bottom lands and islands which are subject to submersion are free from danger. Wilson and Chowning named the disease *Piroplasmosis hominis.* Later investigations, except that of Anderson, have failed to confirm their view and the disease is not now considered a piroplasmosis. The causative organism is not known.

A consideration of the etiology of the two diseases shows many points of resemblance, but also some important differences. Both occur in small and usually strictly limited areas along certain streams running through mountainous country. The district in each instance is subject to heavy snowfull in winter and the streams to spring or summer floods. Along each infected stream the dangerous spots are usually more or less uncultivated and the soil overgrown with underbrush, trees or weeds, while the immune spots are well cultivated. In each country the disease is attributed to the bite of an *Acarina,* and in each a supposed protozoön blood parasite has been described as its cause, but has not been confirmed as such. Contagion is unknown in either disease.

The differences in the etiology of the two infections are equally well marked. The *Acarina,* the bite of which causes *tsutsugamushi,* is always a six-legged, larval *Trombidium,* the adult form being unknown. The insect conveying "spotted or tick fever" of Montana is always *Dermacentor occidentalis,* and usually the adult. *Tsutsugamushi* disease always occurs *after* floods, being contracted on ground which has actually been submerged by the swollen river. Fields immediately adjoining the infected areas and but a few feet higher are considered safe. The Montana disease may precede the flooding of the streams or, more usually, accompanies it. It is very commonly contracted on ground which has not been submerged, but which is on hillsides high above the level of the river. The cases begin in March and rarely appear after the middle of July; *tsutsugamushi* disease beings to appear in July and continues to occur until some time in October.

Spotted-fever regions are uncultivated either because of the elevation and roughness of the land and the difficulty of irrigating it, or of the relative newness of the country. Regions infected with *tsutsugamushi* disease are uncultivated because of their low and flat positions, which subject them to annual floods which destroy most crops, and because, for an immemorial period, they have been recognized as dangerous.

V. SYMPTOMS.

Tsutsugamushi disease is not usually preceded by well-marked prodromata. Occasionally there may be a few days of malaise and indisposition, but its common history is that in from five to twelve days, reraly less than five, after the receipt of a bite from a red mite the patient has a chill; headache and fever follow and a group of lymphatic glands, usually those of one axilla or groin, are found to be enlarged, painful and tender. Examination of the region drained by these glands leads to the discovery of the lesion resulting from the bite. This lesion is small, circular and usually 2 to 4 millimeters in diameter. Some writers state that in its early stages the lesion is a small vesicle. In most instances it is a black or brown area of necrosis of the derma. The dark necrotic skin is very adherent, but after a varying number of days it loosens and is cast off, leaving a circular, punched-out ulcer of slightly greater diameter. The periphery of the ulcer is pinkish in color, slightly infiltrated and generally it is not painful or tender. Enlargement of the lymph vessels connecting the lesion and the large and painful glands can not be detected. The glands, while enlarged and inflamed, do not present great swelling, are not fused together, and are movable beneath the skin.

The temperature at this early stage ordinarily runs from 38°.2 C. (101° F.) to 29°.6 C. (103° F.). Tanaka states that it may reach its maximum in twenty-four hours. The pulse is from 80 to 100 and strong.

The conjunctival vessels are often injected, slight cough may be present, the tongue is moist and somewhat coated, the bowels constipated, and slight or moderate splenic enlargement demonstrable. The urine may contain albumen and the diazo-reaction is present. The patient ordinarily feels comfortable, if headache be excepted and the appetite may be surprisingly good.

As the disease advances, the above symptoms become more marked. General, slight enlargement of superficial glands occurs, the temperature reaches 40° C. (104° F. to 40°.5 C. (105° F.) and is continuous. The pulse weakens and quickens and it may become dicrotic; the first heart sound may be impure. The presence of albumen and the diazo-reaction in the urine are more marked and casts may be numerous; injection of

the conjunctivæ and lachrymation are more evident; respiration is accelerated, the breath sounds are harsh, cough increases and may be harassing, although the expectoration is scanty. The entire surface of the body is apt to be hypersensitive and this condition causes complaint. Constipation usually persists, but exceptionally diarrhœa and abdominal pain and tenderness occur. The tongue becomes dry, brown in the center and glazed at the tip and edges, sordes collect and the gums may become spongy and bleed. In such cases the breath is particularly foul. Partial deafness occurs, the patient becomes stuporous and may pass into coma before death. At some period of the disease, usually from the fifth to the seventh day, although it may be a little earlier or later, an exanthem appears, first on the face and later on the chest, the forearms, the legs and the rest of the trunk; occasionally the palate and buccal surfaces also show it. The eruption consists of irregular, rather faint, dusky or pink macules or flattened papules 2 to 5 millimeters in diameter, which may become confluent on the cheeks and give an appearance of swelling. On the relatively dark skin of a Japanese, this eruption is not well shown, and on parts of the body other than the face the lesions bear a great resemblance to flea bites, with which they may be confused. They fade on pressure, but at once return when it is removed. The eruption does not itch and its duration usually is from four to seven days, although at times this period may be more or less. The eruption never becomes hæmorrhagic or petechial. Tanaka states that in rare instances it may become vesicular or pustular, but this condition is probably less frequent than his implication would lead one to believe. The period of exanthem marks the height of the disease and as the eruption begins to fade, usually about the end of the second week, the fever lessens and in a few days the temperature reaches the normal, while the general condition also rapidly improves. The patient then speedily recovers, although the little ulcer resulting from the bite may be long in healing.

The above description gives the symptoms of a case of average severity which recovers; in more severe ones which recover, the fever may last longer and the symptoms be very marked. In severer cases still, death may result on from the ninth to the fifteenth day. On the other hand, very light infection may show but slight and ephemeral fever, very trifling or no exanthem, and may not be bedfast. Nevertheless, the ulcer and lymphatic enlargement are always present and the former may be larger than usual, having a diameter of as much as 1 centimeter. The duration of the disease is usually about three weeks. It may be as long as a month or as short as one week. Parotitis, melæna and mania have been noted as complications, while coma, cardiac weakness and pulmonary œdema may be terminal features.

Spotted or *tick fever*, as it occurs in the Bitter Root Valley, begins in from one to eight days after the tick bite, in cases where the history of bite is obtainable. As in *tsutsugamushi* disease, prodromata are

unusual, the sickness commonly commencing with a chill. There is not the constant signal symptom of localized lymphadenitis which enables one to find the tick bite, and when it is present it is usually due to pyogenic or other infection of the wound, and lymphangitis may accompany it, while the margins of the lesion are more inflamed and indurated than in the other disease. In many cases no tick bite can be located. When found it does not present the constant appearance of a small, round necrotic area succeed by an ulcer as in the case of the mite bite. The temperature in spotted fever is not essentially different from that in *tsutsugamushi* disease, although it does not show the constancy of type shown by the latter; the eye symptoms, constipation and splenic enlargement may be the same.

As spotted fever progresses the symptoms in the main bear a great resemblance to those of *tsutsugamushi* disease, with the following exceptions:

a. The fever in the latter disease is more typically continuous; in the former more irregular.

b. The pulse rate in spotted fever as compared with the temperature is apt to be relatively high; in *tsutsugamushi* disease it may be the opposite.

c. The majority of spotted-fever patients are dead before the end of the second week.

d. As a rule, the exanthem in spotted fever appears earlier than that of *tsutsugamushi* disease. It shows first on the wrists and ankles and rapidly spreads to cover the entire body. It is much more abundant and more plainly visible than that of *tsutsugamushi* disease, although the latter fact is doubtless related in part to the darker color of the skin in Japanese. It usually consists of macules or petechiæ, although it may resemble the rash of measles or of rötheln; but in practically all cases it soon becomes petechial or hæmorrhagic, and large extravasions may be produced by the confluence of neighboring hæmorrhagic spots. Instead of disappearing in from four to seven days this eruption usually persists until after the patient has died or recovered and slightly pigmented stains may mark its location for weeks on the bodies of persons recovering. Some of the points of extravasation may pass on to gangrene and sloughing, a thing unknown in *tsutsugamushi* disease.

e. Hæmorrhagic extravasation not infrequently takes place into the scrotal tissues of make subjects of spotted fever, never in cases of the other disease.

f. The tongue and lips of the spotted-fever case may be dry, cracked and bleeding, but the gums do not become spongy and do not ooze blood, as is sometimes the case in *tsutsugamushi* disease.

g. Parotitis, malæna and mania have not been noted as complications.

IV. BLOOD EXAMINATION.

So far as we know, no complete studies have been made of the condition of the blood in *tsutsugamushi* disease. Tanaka states that the red cells usually run from 4,800,000 to 5,200,000, the leucocytes from 6,000 to 8,000, and the hæmoglobin from 40 to 75 per cent.

On the other hand, Dr. Miyajima informed us that the red cells fall during the course of the disease to 3,000,000 or 4,000,000, while the

hæmoglobin is reduced proportionately, and he also states that leucopenia obtains. He had not made differential counts of white cells. We were disappointed in not having apparatus for making blood counts and were forced to content ourselves with examinations of fresh and stained films. From such examinations we judge that the red cells are not deformed, that they stain normally, and that the differential white cell count is probably not of much assistance in diagnosis. There is apparently a well-marked leucopenia.

The number of cases examined by us is too small to enable us to draw any general conclusion as to the value of differential counts in the prognosis, but if they indicate anything, it is that they have such value.

It will be noticed that Case 4, discharged recovered, and Case 5, suffering from a third attack and apparently not very sick, both had low polymorphonuclear and high lymphocyte counts; while Cases 1 and 2, both ending fatally, and 3 and 6, both serious, if not fatal, did not show either. So far, then, as a general deduction might be drawn from the consideration of differential counts on six cases, it would appear that a relative decrease of polymorphonuclear and increase of mononuclear cells, particularly of lymphocytes, constitute a favorable prognostic omen. We were unable to recognize parasites in either fresh or stained specimens of blood, except one body in a fresh film from Case 6. The body was intracellular, amœboid, unpigmented and about 1μ in diameter. We believed it to be a young tertian parasite. (Malaria is common in the district.)

The following table shows the results of our differential counts. They are all made on blood drawn August 2, and in each case at least 400 white cells were counted.

TABLE I.—*Differential blood counts in tsutsugamushi disease.*

	Case 1, fatal.	Case 2, fatal.	Case 3, severe.	Case 6, severe.	Case 4, mild.	Case 5, mild.
Small lymphocytes	7	5	8	8	18	18
Large lymphocytes	11	10	7	12	21	27
Polymorphonuclears	74	80	84	77	54	45
Transitional and large mononuclears	8	5	1	3	6	9
Eosinophiles					1	1

In spotted fever, as in *tsutsugamushi* disease, the blood condition has not been studied sufficiently to permit the drawing of general deductions. Wilson and Chowning and Anderson agreed that the red cell counts were reduced about 20 per cent; the hæmoglobin somewhat more; while the leucocytes were increased. In one fatal case, in a pregnant woman, Ashburn found a leucocyte count of 15,600. Not enough differential

counts have been made to enable us to form an opinion as to their value in prognosis. Anderson reports such a count in a recovering case, the percentages being as follows: Small lymphocytes, 9.9; large lymphocytes, 10.6; polymorphonuclears, 78.7; eosinophiles, 0.3.

Wilson and Chowning and Anderson described what they considered a *Piroplasma* in the blood of spotted-fever cases. Later observers have not confirmed this and we do not think that any organism can be seen.

VII. MORTALITY.

The mortality in *tsutsugamushi* disease has been variously estimated at from 15 to 70 per cent or more. Statistics of 567 cases carefully recorded by Dr. Miyajima give an average mortality of 27 per cent. The rate shows a steady and progressive increase from 12.5 per cent in the first decade of life to 57 in the seventh.

The mortality statistics of tick fever are not based on such a large number of cases and it is probable that many of these which are included in Wilson and Chowning's tables, but which occurred prior to 1902, were not really spotted fever. These authors nevertheless figure the percentage of mortality as 75, and that is approximately correct. This disease is therefore more fatal than the other. So far as the statistics at hand give any indication, the mortality does not steadily increase with the age of the patients.

VIII. IMMUNITY CONFERRED BY ATTACK.

One attack of *tsutsugamushi* disease does not confer permanent immunity against another. Probably a temporary immunity is always produced, but second and third attacks in later years are not rare. One of the cases seen by us in August was suffering from his third attack. As a rule, the later attacks of the disease are milder than the first.

In tick fever second and third attacks are unknown and it seems probable that they do not occur. However, the number of living persons who have had the disease is so small as to make generalizations on this point dangerous. Ricketts says that active immunity of at least two or three months' duration is produced in the monkey or guinea pig by an attack of the disease.

IX. SUSCEPTIBILITY OF ANIMALS.

Ogata states that *tsutsugamushi* disease is inoculable into kittens, apes, mice and guinea pigs. Dr. Miyajima, who has done much work on the subject, maintains that it can be produced in monkeys either by mite bite or inoculation from a patient, but not in mice or guinea pigs. Infected monkeys show fever, but not the skin or genital involvement described by Ricketts as occurring in the same class of animals inoculated with spotted fever. Wilson and Chowning thought rabbits

and spermophiles to be inoculable with spotted fever; Stiles and Ashburn were unable to produce the disease in them. Ricketts and King have conveyed the infection to monkeys and guinea pigs, and more recently Ricketts appears to have produced it in the horse.

X. PROGNOSIS.

The prognosis, in view of the mortality, is considerably better in *tsutsugamushi* disease than in spotted fever, and this is particularly true with regard to young subjects. However, in neither disease can much reliance be placed on mild symptoms during the early days of sickness, for in both it too frequently happens that a patient who for some days has had very moderate fever, a good appetite, no pain, and has appeared only slightly or not at all sick, will take a turn for the worse and in a short time be in a very dangerous condition. Later, the patient may die in spite of the fair promise of the early symptoms. Prognosis, therefore, should be guarded. In both diseases pregnant women are liable to abort and die. Judging from the cases here reported, we may hope that the differential leucocyte count will prove valuable in estimating the prognosis in given cases of *tsutsugamushi* disease.

IX. PATHOLOGIC ANATOMY.

The knowledge of the conditions found *postmortem* in both diseases is as yet incomplete, because in the region of flood fever, as in that of spotted fever, there is a sentiment against autopsies and very few of them have been obtained. The only pathologic conditions recognized as characteristic of *tsutsugamushi* disease are the ulcer at the site of the bite, and the moderate lymphatic and splenic enlargement. Œdema of the lungs and hypostatic congestions may be found. The kidneys are swollen and congested and may show acute nephritis.

The findings in tick fever are not greatly different from those given above. The characteristic ulcer and the lymphatic enlargement are not present, whereas the skin lesions are striking and may include large areas of extravasation, or small patches of gangrene. Ricketts's findings of lymphatic enlargement in animals dead of experimental spotted fever indicate that more careful search might reveal such enlargement in human subjects of the disease.

XII. DIAGNOSIS.

Tsutsugamushi disease presents points of resemblance to malaria, typhoid, typhus, pneumonia, and plague; its locality and the season at which the disease occurs are of course important points of differentiation. Examination of the blood for malarial parasites and for the Widal reaction will be of further assistance, as will the absence of most of the physical signs of pneumonia and the presence of the mite bite, the lym-

phatic enlargement and the eruption. The character of the epidemic and the presence of plague bacilli in the sputum, glands or viscera would distinguish the disease from plague. A mild case of typhus occurring in the endemic region at the proper season would possibly be very hard to differentiate. The darker, more profuse and petechial eruption, the absence of characteristic lymphatic enlargement and of the bite and the contagiousness should make the diagnosis reasonably certain.

Spotted or tick fever of Montana bears a much closer resemblance to typhus and, in our opinion, can only be distinguished from it by its seasonal and geographical limitations and its lack of contagiousness. Spotted fever may also present a great resemblance to cerebro-spinal meningitis, from which, in the most nervous cases, it can be differentiated by consideration of season and locality, the more ephemeral nature of the nervous symptoms, the absence of such serious signs as blindness, and the occurrence of other and less nervous cases. Finally, it can be diagnosed by the autopsy. Malaria, with the exception of recurrences of the disease contracted elsewhere, does not occur in the spotted-fever country. Typhoid can be excluded by the blood examination and by the appearance of the rash.

While the wide geographical separation of the two diseases renders it improbable that anyone else will be called upon to differentiate between *tsutsugamushi* disease and tick fever of Montana, it is germane to the subject of this paper here to summarize the points of differentiation by means of parallel tables.

TSUTSUGAMUSHI DISEASE.	SPOTTED FEVER.
Geographical distribution:	
Confined to Echigo and Akita Provinces in Japan.	Confined to parts of the Rocky Mountain region.
Contracted on ground that actually has been submerged.	Contracted on ground that has not been submerged.
Season:	
First of March to end of June (usually).	End of June to October.
Etiology:	
Due to bite of infected larval *Trombidium.*	Due to bite of infected *Dermacentor occidentalis.*
Incubation:	
Five to twelve days (usually).	One to eight days.
Symptoms, early:	
Onset. Usually by chill, followed by headache, malaise.	Same. Headache and backache more common.
Pain and swelling of lymphatic glands on first or second day leads to discovery of bite.	Not so. Tick bite, if present, may be inflamed.
Bite always present and demonstrable. Shows small black area of necrosis.	Not so. When present it is usually a red mark.

TSUTSUGAMUSHI DISEASE—continued.	SPOTTED FEVER—continued.
Symptoms, early—Continued.	
Superficial lymphatic glands become enlarged elsewhere than near wound.	Not so.
Temperature 38°.3 C. (101° F.) to 39°.5 C. (103° F.).	Not so constant.
Injection of conjunctivæ and photophobia are frequent.	Same.
Nose and *throat* normal.	Sore throat occasional.
Tongue moist, slightly coated.	Same.
Constipation.	Often present, but not as a rule.
Spleen enlarged.	Same.
Symptoms, later:	
Fever to 40° C. (104° F.) or 40°.5 C. (105° F.), continuous.	More irregular and may be higher or lower.
Pulse may be slow, but is usually rapid and weak. May be dicrotic.	Almost always rapid and weak. May be dicrotic.
Exanthem usually fourth to seventh day. First on face and temples.	Usually second to fifth day. Usually first on wrists and ankles.
Indistinct or absent on thighs and arms.	Not so.
Macules or papules, dusky.	Macules or petechiæ.
Usually lasts four to seven days.	Fades more slowly.
Does not become hæmorrhagic.	Becomes hæmorrhagic.
Frequently shows in mouth.	Not so.
Hyperesthesia common through disease.	Often present.
Partial deafness frequent.	Less frequent.
Tongue and lips may crack and bleed.	Same.
Gums spongy, may ooze blood.	Not so.
Cough may be severe and paroxysmal, expectoration tenacious.	Cough common, and œdema of lungs common at end.
Perspiration common.	Not noted. Skin often dusky or marbled.
Remission at end of second week.	No constancy. Most patients dead before that.
Ulcers may be long in healing and glands remain tender.	No such condition.
Complications:	
Parotitis, malæna, mania.	Not noted.
Coma, cardiac weakness, pulmonary œdema.	Frequent.
Mortality:	
30 per cent. Increases steadily with age.	75 per cent. No steady increase with age.
Pathological anatomy:	
Ulcers, lymphadenitis, large spleen, hypostatic congestions. May be nephritis.	No ulcers. Lymphadenitis not noted. Large spleen; hypostatic congestions. May be nephritis.
Immunity:	
Not conferred by attack.	Probably conferred by one attack.

XIII. PROPHYLAXIS.

The only prophylactic measure which as yet has been put to any general use against either disease is avoidance of the infected regions. This is much easier in the case of *tsutsugamushi* disease than in that of spotted fever, because the dangerous regions are so much smaller and are plainly marked off by the very flooding that makes them dangerous, and moreover they are not residence sites. Some of the Japanese investigators are recommending that persons who are compelled to enter the dangerous regions should wear clothing saturated with petroleum. The use of carbolic baths, benzine, oil of peppermint and balsam of Peru are also advocated. The effectiveness and applicability of these measures remain to be proved. It is stated that cultivation of the soil and the use of human fæces as manure will free an infected area from the disease in about three years, if its submersion meanwhile is prevented.

XIV. TREATMENT.

So far as personal observation enables us to form opinions on this subject, it indicates that the treatment in both diseases is divisible into two classes:

1. Expectant-symptomatic.
2. Hoped-for specifics, which are apt to be the result of guesswork or of reasoning from false premises or erroneous observations.

The clinical symptoms of both diseases and the results of practice in clinically similar diseases, such as typhoid and typhus, indicate that each offers a field for a more extended use of hydrotherapy than either has yet received.

XV. CASE HISTORIES OF TSUTSUGAMUSHI DISEASE.

The following are such histories and notes as could be obtained in regard to the cases of *tsutsugamushi* disease seen by us this year:

CASE I.—*S. Igarashi; male; age, 17 years; farmer.*

Family history.—Negative as regards *tsutsugamushi* disease.

Personal history.—Patient had been in the infected locality at various times and does not know when he was bitten by mites. This is his first attack of the disease.

Present illness.—The disease began on July 24, 1907, with a chill. The next day the patient entered the hospital. At that time the glands of one axilla were enlarged and tender, and examination of the region drained by them showed the small ulcers resulting from three bites. There was no skin eruption and the spleen was not demonstrable. The pulse was strong, frequent and regular, appetite decreased and the bowels constipated. Urine was normal. The temperature is shown by Chart 1.

On July 26 an eruption of rose-colored macules appeared on the face. Later it gradually spread over the body and limbs. The diazo-reaction was well

marked in the urine of July 28, and the pulse was that day dicrotic. The eruption showed on the hard palate and the fauces, and some cough was present.

August 1: The present condition is indicated by the foregoing notes, there having been no change.

August 2: The patient is sluggish and stupid. The eruption is still present but is not prominent; the eyes are injected and suffused, the spleen is tender but not palpable; respiration is rapid and the pulse feeble. The patient sleeps well and has had no delirium.

August 3: The urine contains considerable albumen and numerous coarsely granular casts. The patient sleeps much and perspires freely, the pulse is 85 but very weak, the heart sounds feeble. There is no cough; breath sounds everywhere harsh. The eruption still shows on the face and chest, but is fading. The eyes are much injected. The tongue is dry, white in the center, glazed at the margins, the papillæ prominent; gums spongy; spleen tender, but not palpable.

August 4: The general appearance and condition are about as yesterday. The gums are very spongy and are bleeding. Cough is present and produces a scant, tenacious sputum, much discolored with blood from the gums. Respiration is rapid and somewhat irregular, the breath sounds harsh. The pulse is rapid, irregular and of low tension, the first heart sound feeble. There is slight œdema of the feet. The eruption remaining on the face is papular and the apex of each papule shows a minute scab; the conjunctivæ are much injected.

August 7: Dr. Craig and I left on the 5th to visit another infected region and on our return this morning we learn that the patient became progressively worse and died on the morning of August 6 with high temperature and œdema of the lungs. Autopsy was not obtainable.

CASE II.—*I. Hasigawa; female; age, 13 years.*

Family history.—Negative as regards this disease.

Personal history.—The patient has been in the *tsutsugamushi* infected region and was bitten by a red mite on July 17, 1907. This is her first attack of the disease.

Present illness.—On July 22 she had a chill and next day entered the hospital. At that time she had fever, a flushed face, weak and rapid pulse, poor appetite, and diarrhœa, the last a very unusual symptom. The left femoral glands were enlarged, painful and tender and just below them was the small ulcer resulting from the mite bite. It was surrounded by a slightly infiltrated, pink border.

On July 27 the spleen was demonstrably enlarged and the urine gave the diazo reaction. It contained no albumen. The patient was delirious at times and was extremely hypersensitive. The temperature is shown by Chart 2.

August 1: Eruption appeared this morning for the first time, showing on the face. It is rubeolar in appearance, but scanty. Diarrhœa has ceased under treatment. The pulse is growing weaker. Cough is present, but unproductive of aught save pain, breath sounds everywhere harsh.

August 2: The patient slept well last night and is not delirious. The pulse is rapid and feeble; cough persists and causes abdominal pain; hyperæsthesia is very marked, and pain causes the patient often to moan. The abdomen is particularly painful and tender, but is not distended or rigid. The bowels are loose. There is a dusky, faint, scattered, macular eruption on the face, arms and legs. Tenacious mucus in the throat excites cough and nausea.

August 3: Face dusky, eyes congested, eruption less distinct; tongue dry and glazed and its papillæ prominent. Hyperæsthesia, abdominal pain and diarrhœa persist. Patient slept poorly last night and is delirious. Respiration rapid and

moaning; breath sounds harsh; cough less severe and distressing. Pulse recorded as 85, but during examination it was 140 and weak. Heart sounds rapid and weak, but clear.

August 4: The patient died at 6 a. m. to-day. Delirium had ceased, but diarrhœa persisted and the heart became rapid and weaker until death occurred. Autopsy was not obtainable.

CASE III.—*H. Itagake; male; age, 14 years.*

Family history.—Negative as regards this disease.

Personal history.—The patient has visited the infected regions and was bitten by a mite on July 19. This is his first attack of *tsutsugamushi* disease.

Present illness.—The disease began with a slight chill on July 27. Since that time the patient has had moderate fever and enlargement of the lymphatic glands, particularly of the right axilla, but has felt comfortable and has not appeared to be very ill. The temperature is shown by Chart 3.

August 1: The patient has had no symptoms except the fever, slight headache and constipation, and does not appear or feel very ill. There is no eruption and the spleen is not demonstrably enlarged. The right axillary glands are swollen and tender and the skin of the same axilla shows a small ulcer with pinkish, slightly indurated and tender margins.

August 2: Face clear and bright. No eruption present and the patient appears well. The tongue is white, slightly dry and tooth-marked. The pulse is of good strength.

August 3: The face is flushed, the eyes injected, a faint eruption present. The patient appears worse than he did yesterday, but does not complain. The tongue is moist and has a white coating, the spleen somewhat enlarged and tender, but not palpable. There is no cough, but the breath sounds are harsh, especially at the apices of the lungs. The urine shows a trace of albumen and very numerous, coarsely granular casts and small round epithelium, but no blood. Examination of the fæces shows *Ascaris* eggs, but is otherwise negative.

August 4: The skin is hot, the face flushed, eyes injected, expression somnolent. The tongue is somewhat dry, red at the margins, and has a thick, yellowish white, central coat. The gums are normal. Cough is present, but there is no expectoration. Respiration is rapid and regular, the breath sounds harsh. The pulse is rapid, compressible and regular; the first sound of the heart roughened over the base and apex.

August 7: On our return to the hospital we learned that the patient had grown worse and had become very nervous, and that he had left the hospital on August 6. His subsequent history is unknown to us.

CASE IV.—*S. Asai; male; age, 17 years.*

Family history.—Negative as regards this disease.

Personal history.—Patient has been in the infected regions, but was not aware that he had been bitten by mites. On July 27 he felt listless and feverish and on the 29th he came to the hospital. At that time he had fever (see Chart 4), his face was flushed and he complained of headache and pain in the pharynx. The lymphatic glands in the left axilla were swollen and painful and careful examination revealed the presence of two small ulcers, one in the left axilla and one back of the hair line of the left frontal region.

August 1: Condition as at time of admission. No eruption has shown and the patient looks and feels well. Spleen not palpable or tender. Slight systolic roughening is noticed over base and apex of the heart. There is slight enlargement

of the superficial lymphatic glands, more marked in the left axilla. Physical examination is otherwise negative.

August 2: The patient looks and feels well, has a good appetite, no pain, no eruption, and sleeps well. The ulcer on the head has healed.

August 3: The patient looks and feels well. The systolic roughening persists unchanged.

August 4: Discharged from hospital, recovered.

CASE V.—*T. Suzuki; male; farmer; age, 44 years.*

Family history.—One son had this disease two years ago.

Personal history.—The patient had an attack of *tsutsugamushi* disease at the age of 17 years and a second one at the age of 25 years. Lately he has visited the infected region, but he does not know when he was bitten by a mite. On July 28 he began to suffer from malaise and he came to the hospital on the 30th. At that time he had fever (see Chart 5) and the right inguinal glands were enlarged, painful and tender. At the right margin of the umbilicus was a very small ulcer with red, puffy edges and covered with a thin crust. There were no other symptoms.

August 1: Enlargement of the epitrochlear glands is noticed, but they are not tender. Patient feels well and appears so. Physical examination is negative.

August 2: There has been no change since yesterday. The spleen is not demonstrably enlarged, the tongue is moist, clean at the edges, and shows a white, central coat; there is no eruption; the bowels are sluggish.

August 3: There is no change in the general appearance or condition.

August 4: There is no marked change. The patient eats and sleeps well, and, except for his fever, the ulcer at the umbilicus and the lymphatic enlargement, appears to be well. The bowels are moving naturally.

August 5: The patient to-day insisted on leaving the hospital, and did so notwithstanding the persistence of fever and the remonstrances of his attendants. The subsequent history of the case is unknown to us.

CASE VI.—*Male; age, 8 years.*

Family history.—The patient's mother had *tsutsugamushi* disease twelve and his father two years ago, both recovering. An employee living in the same house also had it at one time, but the date is unknown.

Personal history.—The patient has at times been fishing in the infected region, but does not know of having received any bite from a red mite. On July 30 he had a chill and since that time has had fever.

August 2: The patient was this morning brought to hospital for the first time by his father. He has a temperature of 39°.5 C. (103°.2 F.) and severe headache. The post auricular and upper cervical glands of the left side are enlarged, tender and painful. Examination shows a mite bite just to the left of the sagittal suture at the vertex. It is a small, brown circle of necrotic skin, about 2 millimeters in diameter. The brown, necrotic tissue is loose at the margins, but most intimately adherent by its under surface to the sound scalp. The tongue has a white coat, through which the papillæ project red and prominent. The eyes are not red or inflamed. Scattered over the face is a slight eruption, which first appeared last night. It is most prominent on the cheeks and consists of faint, dusky macules, 2 to 5 millimeters in diameter, which fade on pressure and return very promptly when the pressure is relieved. The spots present the slightest perceptible degree of elevation. There is no eruption in the mouth or throat. The spleen is enlarged, the appetite poor, the bowels constipated; there is no cough and the heart and lungs are normal. Removal of the necrotic area of the bite

by means of forceps and scissors leaves a small ulcer with steep margins and a whitish or grayish lining, the appearance of which is said to be very characteristic.

August 7: The patient did not enter the hospital and we have seen him but the one time. We are told that his fever is high and his condition serious. The subsequent history is unknown to us.

CASE VII.—*Sakuma; male; farmer; age, 20 years.*

Family history is negative as regards *tsutsugamushi* disease.

Personal history.—The patient has not had this disease previously. On July 27 he was bitten by a red mite. On August 3 he was taken sick with fever and a feeling of uneasiness. He continued feverish, but had no great discomfort, nor any marked symptoms, and came to the hospital on August 5. The maximum temperature that day was 40° C. (104° F.), the highest pulse rate 94. On August 6 the highest temperature was 39°.5 C. (103°.2 F.), the highest pulse rate 107.

August 7: We saw the patient for the first time this morning. He has a temperature of 39° C. (102°.2 F.), and a good pulse of 95. There is slight enlargement of the superficial lymphatic glands, most marked in the left axilla, where they are also tender. The bite is located in the left axilla and is an ulcer with a mass of black, necrotic tissue still attached to its central part. It is larger than usual, being about 1 by 0.5 centimeter. The conjunctivæ are congested, the tongue moist and white and an eruption is present this morning for the first time. This is most marked on the right cheek and consists of six dusky, very slightly elevated papules which fade on pressure. The bowels are regular and the patient has neither cough nor pain. He sleeps and eats well, but his expression is somewhat dull and listless. The spleen is slightly enlarged, but neither tender nor palpable. The examination of heart and lungs is negative.

We did not see this patient again and know nothing of his subsequent history.

XVI. CONCLUSION AS TO THE NONIDENTITY OF THE TWO DISEASES.

We think that a consideration of the facts concerning the two diseases, as at present known and set forth above, justifies the opinion that they are separate and distinct disease entities. They present many points of resemblance, but those are not sufficient to overbalance those of difference.

XVII. DOES TSUTSUGAMUSHI DISEASE OCCUR IN THE PHILIPPINE ISLANDS?

The ready answer which the large majority of medical men in the Islands would give to the above question would be in the negative and it is probable that they are correct. Nevertheless, certain cases are seen which should lead to a more complete investigation of the subject. In these Islands there occur a great many cases of anomalous fevers and these are probably of several kinds. In our report for the quarter ending June 30, 1906, we made passing reference to two which were seen by one of us at Camp Connell, Samar, in the preceding February and we are in possession of the temperature charts and the notes made on them by First Lieut. Earl H. Bruns, assistant surgeon, United States

Army. These cases bear considerable resemblance to those of *tsutsugamushi* disease and therefore it seems advisable to refer to them again and more at length.

Before discussing them it is well to mention the climatic conditions under which they occurred. Camp Connell is located on the west coast of Samar and lies but a few feet above sea level. At one side is a low, flat stretch of land that was formerly a swamp, but it has been drained and made into a target range. In time of very heavy rains water still covers the range and it may be submerged for two or three days at a time, or such was the condition in 1905 and 1906. The ordinary annual rainfall at the post is about 330 to 400 centimeters, and almost all of the precipitation occurs between the first of June and the first of January. During January the target range generally becomes dry and hard. In 1905 the post suffered from drought, which began in January and was not fully relieved until late in May. In 1906 there was again very little or no rain in January and a repetition of the condition of the previous year was feared at the time that these cases occurred. The condition of the target range in December, January and February is somewhat similar to that of the *tsutsugamushi* infected regions in Japan in June, July and August.

One of us (Ashburn) happened to be at Camp Connell investigating the question of water supply in February, 1906, and was asked to see the two cases to be quoted, because of their resemblance to the spotted fever of Montana. The notes to follow were made by Lieutenant Bruns eighteen months before we saw any sufferers from *tsutsugamushi* disease or considered the possible relationship between the two infections.

CASE A.—*D. L. C.; age, 29; private, Company M, Twenty-first Infantry.*

Family history.—Negative.

Personal history.—The patient has had the usual diseases of childhood, pneumonia at 9 years and at 14 years of age, dysentery in 1901, malaria in 1901, gonorrhœa and chancroids in 1905.

Present illness.—January 29, 1906: For the past six days he has had headache and pain in the back and has been feverish and constipated, but has had no chill. He was admitted to the hospital this morning with the following symptoms and signs: Headache, pain over the kidneys, constipation, slight pain in right iliac fossa, slight, dry cough; heart, lungs, liver and spleen normal. There is an eruption of flat, rose-colored, irregular macules scattered over the chest, abdomen and legs, and about the anus. General glandular enlargement is present, the right femoral glands being also painful and tender. (See Chart A.)

January 30: No malarial parasites in blood; leucocyte count 5,400; urine normal.

January 31: Glands in right femoral region more enlarged, tender and painful. There is headache and slight abdominal pain.

February 2: Muttering delirium, nervous twitching and subsultus are present this morning. The skin is mottled and the eruption increased on chest, abdomen, neck, face, legs and about the anus. Tongue coated and dry, pulse dicrotic. Femoral glands smaller.

February 3: Breathing is thoracic and shallow, face flushed; femoral glands painful; eruption more dusky. The pulse is rapid and irregular.

February 4: No change. Blood shows no malarial parasites; leucocyte count, 4,300.

February 6: The patient feels better this morning; the pulse is of good tension, the eruption fading.

February 9: Improved. Patient looks brighter and feels very well. His mental condition is peculiar, not normal.

February 10: Delirious all night and to-day. Face flushed; pulse remains fairly strong.

February 11: Improved, quiet no pain.

February 13: Improved, hungry. The pulse is good and the rash disappearing. Urine normal.

February 16: The patient has improved. He has no pain, the pulse is strong, the eruption and glandular enlargement have disappeared.

February 19: The Widal reaction is negative after one hour.

CASE B.—*H. D. P.; age, 34; teamster.*

Family history.—Negative.

Personal history.—The patient has had diseases of childhood, "typhoid-malaria" in 1894, dysentery in 1903. There is no history of syphilis or gonorrhœa.

Present illness.—February 2, 1906: The patient has felt badly for five days and has had headache, pain in the back and limbs and in abdomen, and the appetite has been poor. There was no chill and but slight cough. Two days ago he noticed enlarged glands in the right axilla and right groin. Yesterday he had diarrhœa. He was admitted to the hospital to-day suffering from fever, pain in the head, back, legs, anus and abdomen, enlarged and painful lymphatic glands in the right axilla and groin, and diarrhœa.

Physical examination.—The heart is normal; dry râles are heard over the upper lobes of both lungs. The abdomen is tender around the umbilicus, the spleen enlarged. A rose-colored, irregular, macular rash shows on the head, trunk and limbs. There is a general enlargement of the superficial lymphatic glands, more marked in the right axilla and groin. The tongue is moist and has a white, central coat and red edges. No malarial parasites found in the blood. (See Chart B.)

February 3: No malarial parasites. The patient is dull, the face flushed, the axillary and inguinal glands painful.

February 4: There is no change. Leucocyte count, 3,200; no malarial parasites.

February 5: The patient appears better this morning. The pulse is of good tension, the eruption fading. There was a marked chill after a plunge bath.

February 6: The eruption is fading, the pulse is good, the tongue dark and dry. No malarial parasites in the blood. A differential count of white cells shows: Small lymphocytes 20, large lymphocytes 8, polymorphonuclears 60, eosinophiles 2, transitionals and large mononuclears 4, per centum.

February 9: Still improving. A gland was removed from the right groin for examination.

February 10: Improving. Face flushed, eyes injected, mouth dry, and the tongue shows a yellowish coat. The pulse is of good tension, the eruption confluent and fading. No malarial parasites in the blood.

February 12: Patient is still improving. He sleeps well. Bacteriological examination of the excised gland was negative.

February 13: The patient is hungry, the eruption has disappeared, the glandular enlargement is less marked and the urine is normal.

February 19: Patient is still improving. Widal reaction was negative after one hour. No malarial parasites found in the blood.

Lieutenant Bruns made daily notes on these cases, but when there was no change in the condition or no new examination mentioned, the remarks have been omitted. Both patients received cold baths during the progress of the disease and the charts are probably modified by them. While the notes do not indicate it, such is probably the explanation of the two marked drops of temperature shown by Charts B. A satisfactory diagnosis was never made on either case, although both were reported as being typhoid fever.

We do not maintain that these cases were *tsutsugamushi* disease, but they certainly present enough points of resemblance to it to make it worth while for medical men in the Philippines to keep the matter in mind, should they have the opportunity of investigating similar infections.

ACKNOWLEDGMENT.

We desire to express our thanks to those assisting us in this study, and particularly to Professor Miyajima and his fellow-workers from the Imperial Institute for Researches of Infectious Diseases, to whom we are indebted for the opportunity to see what we did of *tsutsugamushi* disease and for such knowledge as we have of the articles published on it in Japanese, as well as for the information they gave us concerning their own work. We are also indebted to Lieutenant Bruns, for his notes on the Camp Connell cases.

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Chart 1.

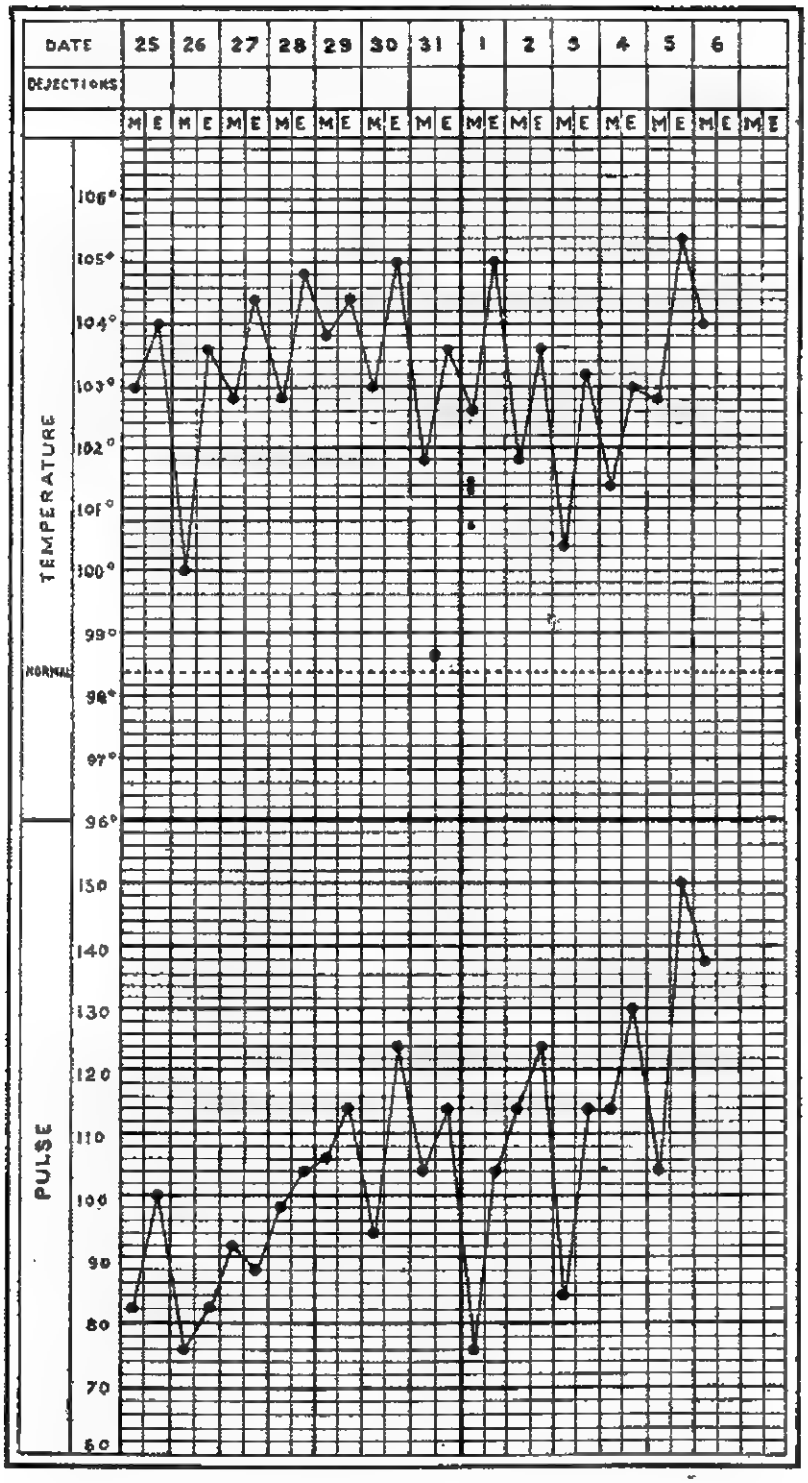
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Chart 2.

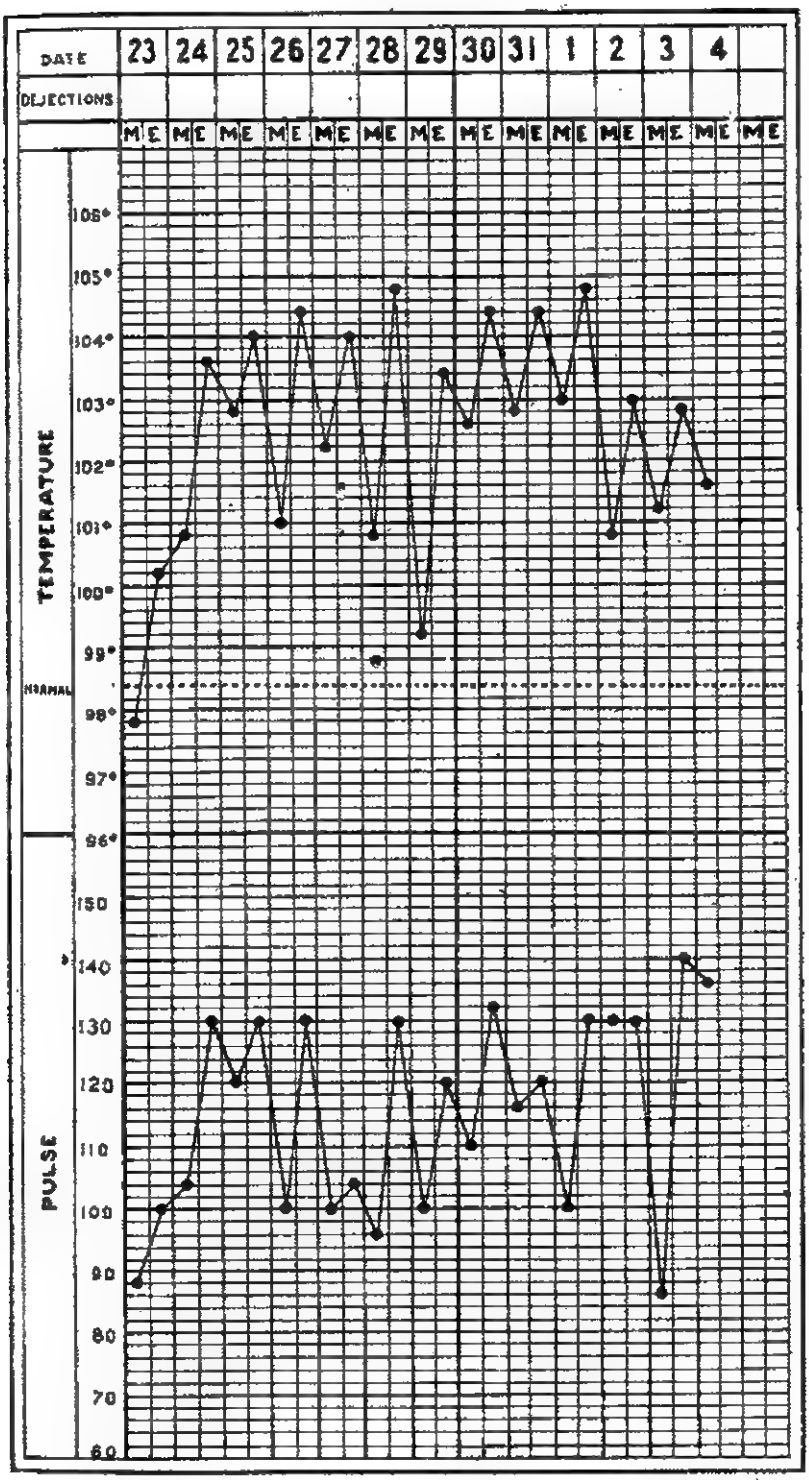
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Chart 3.

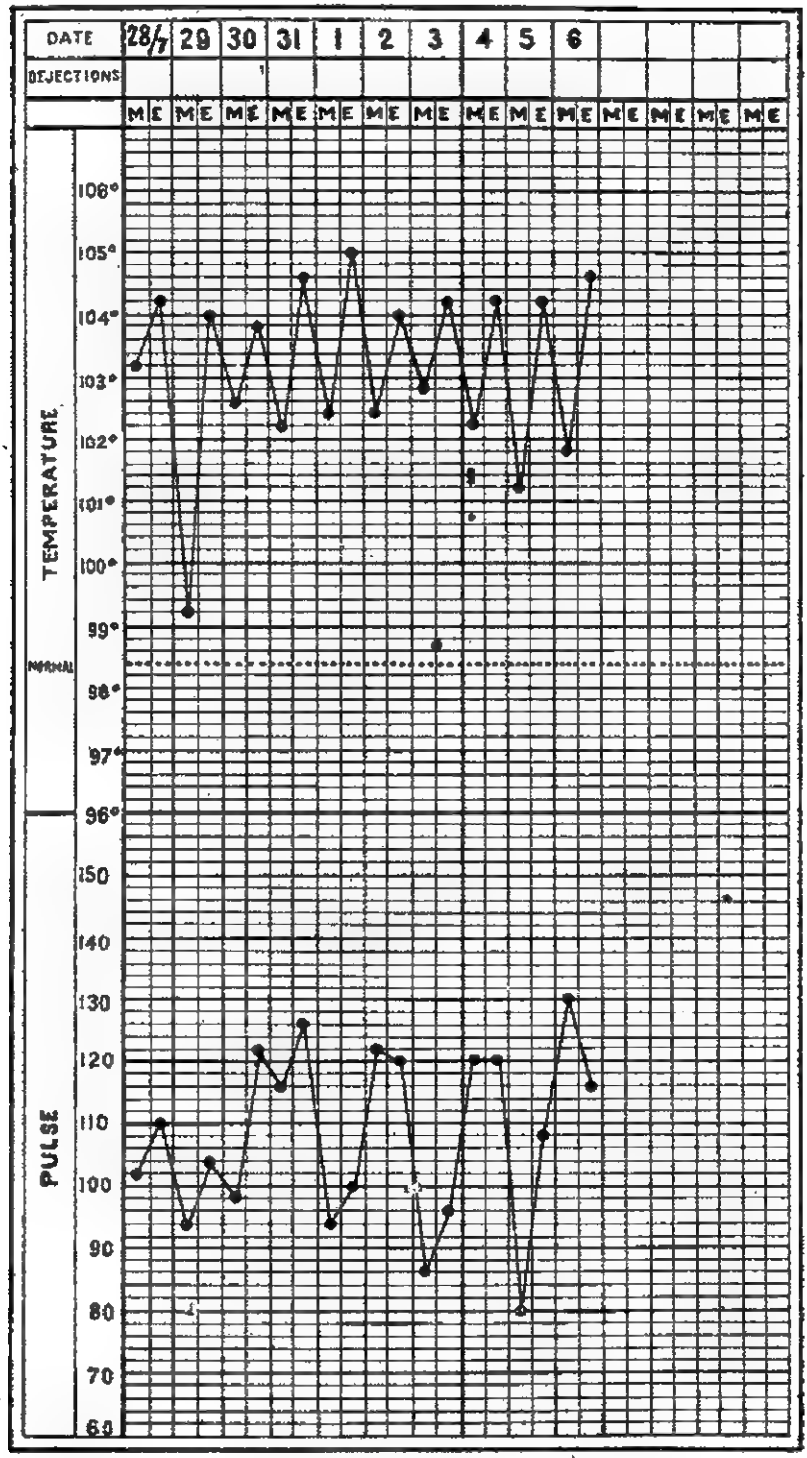
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Chart 4.

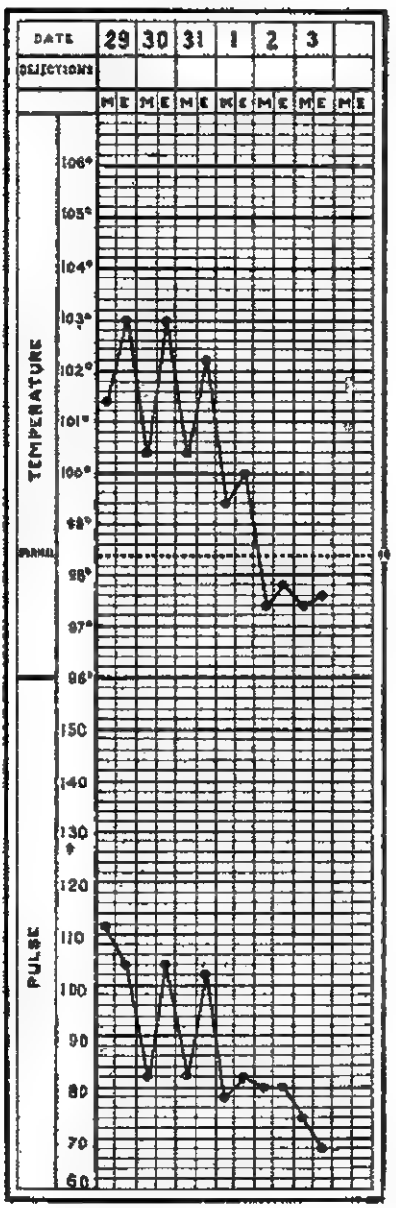

Chart 5.

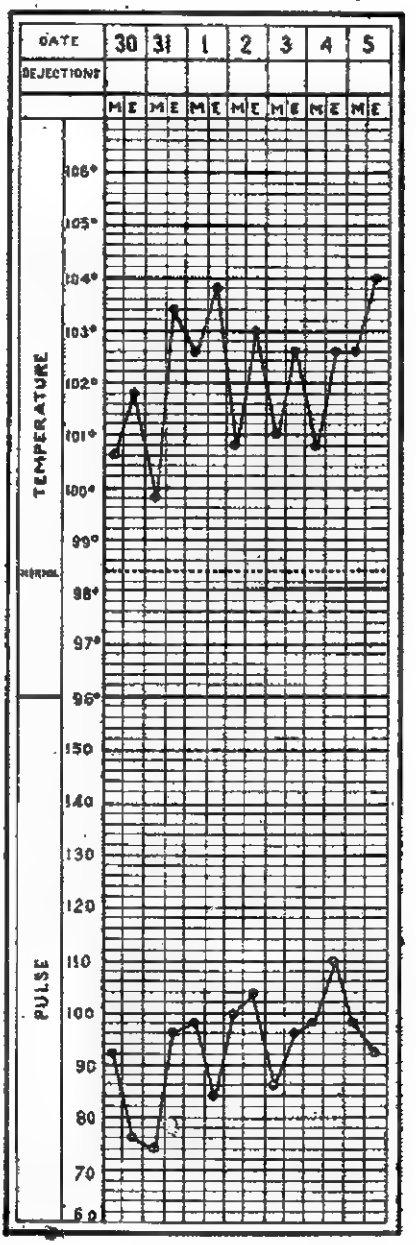

Chart A.

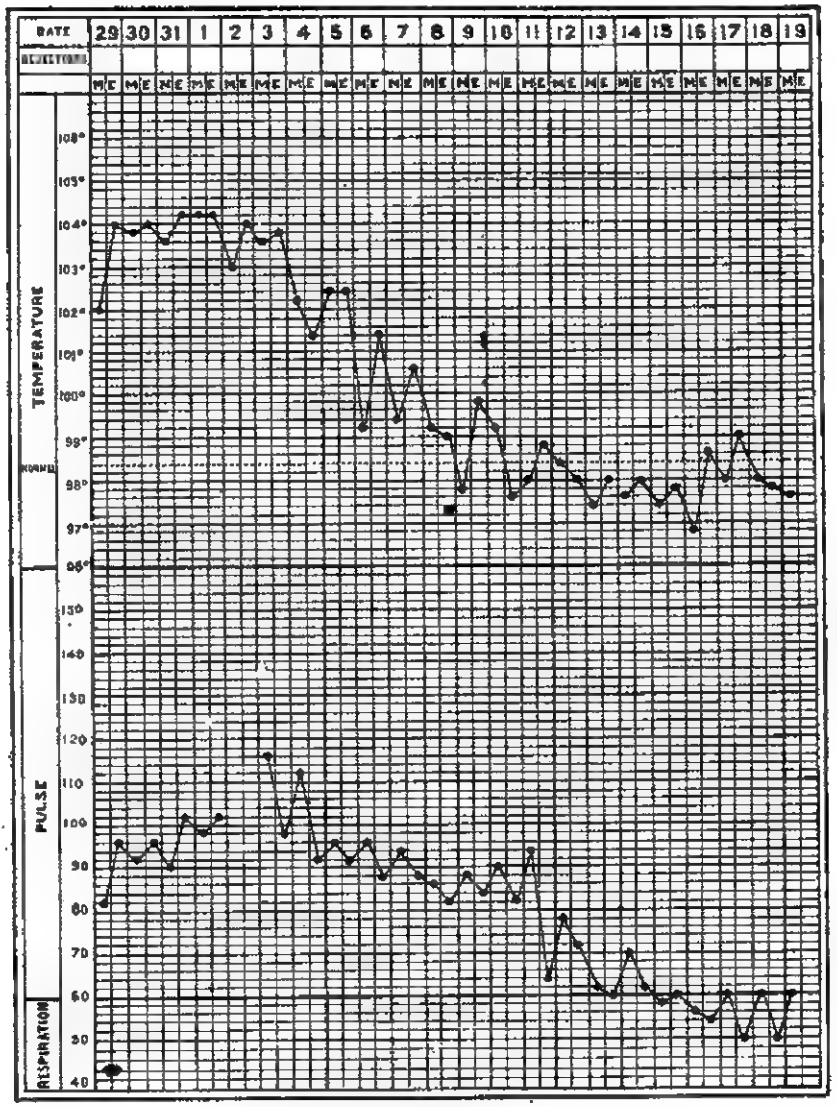
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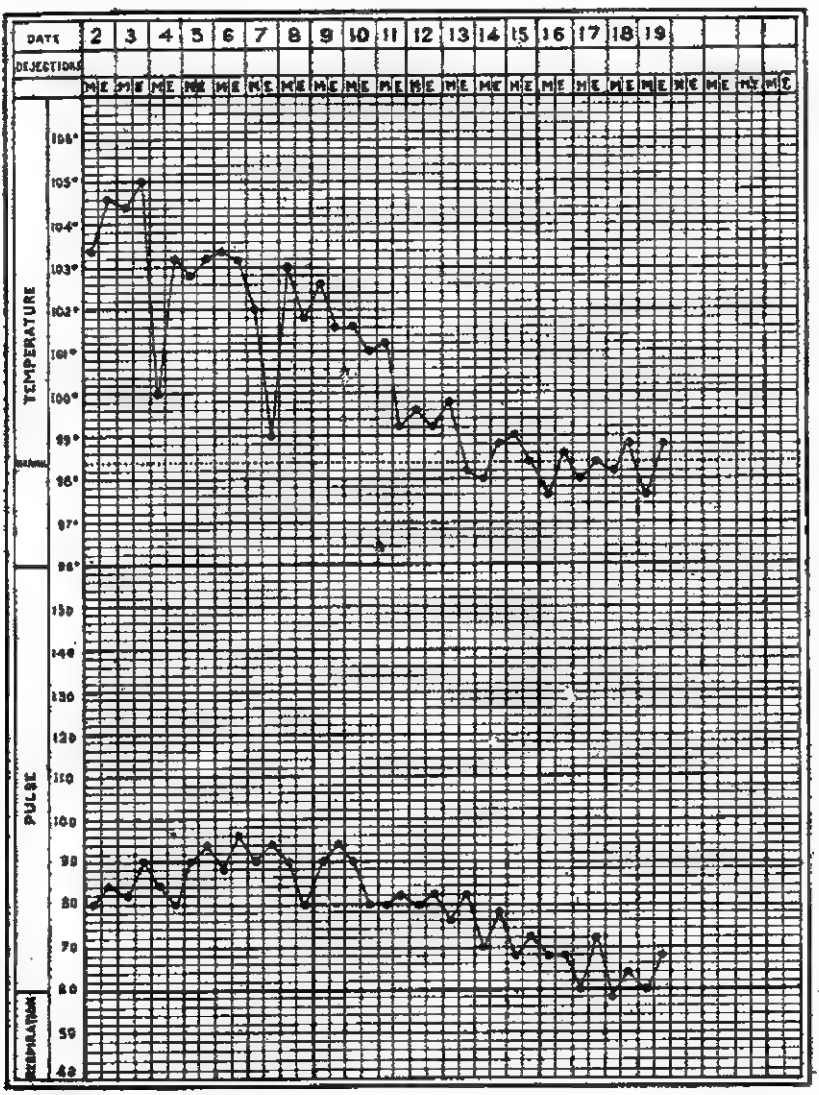
Chart B.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A SERIES OF CASES OF TROPICAL INFANTILE DYSENTERY WITH A HITHERTO UNDESCRIBED BACILLUS AS THE CAUSATIVE FACTOR.

[Preliminary report.]

By FRED B. BOWMAN.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

During the latter part of July and the month of August, 1907, quite a severe epidemic of infantile dysentery prevailed in and around Manila, and the following observations were made upon a series of cases from the private practice of Dr. Musgrave. It was evident, judging from the suddenness of onset, the severity of the attack and the extremely long period of convalescence in some instances, that we were dealing with a severe infection caused by some pathogenic intestinal organism, probably the Shiga bacillus itself or one of the many varieties of *B. dysenteriæ*. It was consequently deemed of importance accurately to study this epidemic and therefore I secured as much material as possible.

In all cases fæcal matter was obtained either in a sterile dish or on a square of sterile gauze, and the specimen were transferred to the laboratory as quickly as possible for examination. A brief history of each case follows, with an outline of the technical procedure adopted in isolating the organism.

CASE I.—*Infant S.*

Severe, acute dysentery with recovery.—A strong, well-developed infant, weighing 8¾ pounds at birth and 19 pounds at 9 months of age. It was breast fed during the first four months and mixed feeding was resorted to until the end of the seventh month. For two months before the attack of dysentery the child was fed entirely on artificial food which consisted of a percentage modification of milk and cream with a small amount of fruit juice once daily. The infant's growth and development were entirely satisfactory before and after the attack. The dysentery developed rather suddenly during the night, the symptoms being cramps, fever and frequent stools. The latter at first were watery and contained mucus, but within six hours they showed small quantities of blood. For the next few days the dysentery was quite severe; it was characterized by pain, tenesmus and fever ranging from 38° to 40° C. During this time the stools were between ten and twenty-five in number during twenty-four hours, consisting almost entirely of blood and mucus. The symptoms gradually subsided and convalescence was

well established on the fifteenth day. The treatment consisted of enemas of 1–2,000 solution of an organic acid peroxide and a very restricted diet, with paregoric in sufficient quantity to control the pain.

Cultures were made from the fresh specimen passed on the morning of the third day of the disease. This was sent to the laboratory contained in a small square of sterile gauze.

CASE II.—*Infant L.*

Moderately severe, acute dysentery with recovery.—The patient was an unusually well-developed, strong, healthy boy 2 years old, weighing 9 pounds at birth and 28 pounds at 1 year of age. Diarrhœa developed, following a period of malaise lasting about twenty-four hours, with about one degree of fever. The character of the bowel discharges rapidly changed to the typical bloody mucus stools of acute dysentery and continued in this manner for about ten days with from six to fifteen passages a day. Convalescence was slow, and complete recovery did not take place until the end of about one and one-half months. At first the prostration was considerable, temperature 38° to 39°.5 C. with a moderate amount of tenesmus and loss of appetite.

The treatment consisted of the same bowel irrigations as in Case I together with occasional doses of castor oil. Pain was controlled by the use of paragoric.

Cultures were made from a fresh specimen of the stool obtained on the second day of the disease.

CASE III.—*Infant B.*

Mild, acute dysentery, with subsequent recurrence and recovery.—A healthy infant 10 months old, breast fed from birth and weighing 22 pounds at the time he was taken sick. Acute diarrhœa suddenly developed during the night and within the next twenty-four hours the stools changed in character to those characteristic of dysentery and so continued for eight or ten days, with from three to ten bowel movements a day. Convalescence was quickly established, but a recurrence similar to the first attack took place at the end of two weeks. Convalescence was again rapid and the child has since remained perfectly well. There was no fever at any time, the tenesmus was not very great and the quantity of blood passed was inconsiderable. There was no loss of appetite and but little toxæmia. After the first two days, the bowel movements could be fairly well controlled by simple irrigation of the colon.

Cultures made on the first day of the disease. No pathogenic organism was found and the bacillus to be described below as present in the two preceding cases could not be isolated.[1]

CASE IV.—*Infant T.*

Severe, acute diarrhœa with recovery.—This infant was 5 months old, weighing 9 pounds at birth. It continued to thrive on breast milk during the first two months. At this time it became necessary to change to artificial food because of failure of the breast supply. From that time until the development of the

[1] Since these observations were made Case III, three months after recovery, developed an acute dysentery similar to the first attack. Bacillus "S" was isolated, being agglutinated by the specific rabbit serum in high dilutions (1–20,000).

diarrhœa, assimilation of food had not been satisfactory. Percentage feeding with a large range of variation in both the proteid and fat content was tried without success. Vomiting was frequent and emaciation became quite marked, so that at the time of the development of the diarrhœa the child was already in a very much exhausted condition. The diarrhœa lasted for about two weeks, with from three to fifteen passages a day, and in a few instances small streaks of blood and a considerable amount of mucus were found in the stools.

Cultures were made on the fourth day of the disease.

The technique used in the first two cases was also employed in this one; it will therefore be unnecessary to give a separate description in each case.

THE ORGANISM.

Smears made from a portion of the mucus of the stool showed two types of bacilli; one a rather large organism with rounded ends, and the other in comparison, extremely small. A series of four alkaline bouillon tubes was inoculated with the material from the mucus portion of the specimen and the tubes were allowed to stand four hours, when a very slight cloud could be observed near the surfaces of the medium. A series of four alkaline agar tubes at 45° C. was made from each tube, plated and placed in the incubator for twenty-four hours at 37° C., when I marked the colonies present; at the end of another twenty-four hours several new colonies had appeared. There were very small and of an intense blue color, the original colonies 24 hours old being creamy-gray. Transfers to alkaline agar were made from each type of colony and placed in the incubator for twenty-four hours, after which time subcultures were made. The results are tabulated below. (See Table I.) I have termed the 24-hour growth "C" and the 48 hour one "S". Stained specimens of bacilli from each tube agreed in morphology with those found in the smears made from the fresh mucus.

Later, after obtaining the reaction of the organism in lactose bouillon, I used another method for its isolation. Fermentation tubes were inoculated directly from the plate colonies, and after the reaction had identified the organism, it was transferred from this medium to agar, subcultures being made from the latter.

A study of Table I shows the following characteristics which distinguish *Bacillus "S"* from *Bacillus coli*. *Bacillus "S"* seems to be somewhat smaller and more delicate than *B. coli*. Its motility is quite marked and is of a wriggling and twisting character. Coagulation is delayed in milk and the litmus present is completely reduced. It forms no gas in lactose-litmus and there is profuse growth. The indol reaction is negative.

Fermentative tests were also made using the colon bacillus isolated from the specimen taken from Case I as a control.

TABLE I.—*Showing cultural characteristics of Bacillus "S" as compared with B. coli isolated from the same stool.*

Bacillus.	Agar-agar.		Glucose-agar.	Lactose-agar.	Gelatin.	Old serum.	Potato.	Lactose-litmus.	Mannite-litmus-agar.	Litmus-milk.	Morphology motility.	Indol reaction.
	½ per cent.	1 per cent.										
Bacillus coli:												
24 hours	Typical colon.	Typical colon.	Much gas, growth.	*Much* gas.	No liquefaction.	Typical colon.	Profuse yellow-brown growth.	Much gas and growth.	Gas, acidified.	Acidified, coagulated, fæcal odor.	Size, 0.7×1.3 μ practically nonmotile. Gram—negative. Stains with all stains.	Positive.
48 hours	do	do	do	do	do	do	do	do	do	do		Do.
72 hours	do	do	do	do	do	do	do	do	do	do		Do.
Bacillus "S:"												
24 hours	do	do	do	*No* gas.	do	do	Almost imperceptible, pure, white growth.	Growth. No gas.	*Much* gas, acidified.	Peptonized, reduction of litmus, no fæcal odor.	Size, 0.5×.075 μ small and thin. Extremely motile. Stains with all the aniline stains.	Negative.
48 hours	do	do	do	do	do	do	do	do	do	do		Do.
72 hours	do	do	do	do	do	do	Heavier growth	Slightly decomposed with gas formation.	Completely decomposed with gas formation and decolorized.	Slight coagulum.		Do.

TABLE II.—*Bacillus "S."*

Media.	24 hours.	48 hours.	72 hours.
Lactose	−	−	−
Maltose	+	+	+
Saccharose	+	+	+
Glucose	+	+	+

The fermentation tubes inoculated with *B. coli* showed more gas in the lactose medium than in any of the others.

PATHOGENICITY.

Transfers were made to slant alkaline-agar tubes and placed in the incubator at 37° C. for twenty-four hours. The slants were completely covered with the growth and each was then in each instance suspended in 20 cubic centimeters of normal salt solution. One cubic centimeter of this suspension (0.05 of an agar slant) injected intraperitoneally, killed a guinea pig in twelve hours, 0.04 of a slant was fatal in less than twenty-four hours. Rabbits were much less susceptible, 0.1 to 0.07 of a 24-hour slant, inoculated intraperitoneally, killing a rabbit in from twenty-four to thirty-two hours. Similar conditions were found in both rabbits and guinea pigs at autopsy, there was injection of the tissues about the point of inoculation, enlargement of lymphatic glands, a large amount of sero-purulent exudate, and both the liver and spleen were congested; stained smears from the exudate and from the liver and spleen showed the presence in pure culture of a small bacillus, identical morphologically with the original organism. Hanging drops of the exudate demonstrated an organism having a marked motility and in some of the specimens examined, an almost cholera-like character. Subcultures made from the exudate developed in a manner identical with that of the original organism. A rabbit inoculated subcutaneously with peritoneal fluid from a guinea pig dead of the infection developed a large, fluctuating abscess and at the same time showed a very marked diarrhœa.

Suspensions of the bacillus in salt solution were fed to a monkey through a stomach tube for four succesive days, after the gastric acidity had been neutralized with sodium carbonate. The monkey became ill, at the end of two weeks the animal was killed and autopsy performed. There appeared to be a certain amount of inflammation of the large intestine and cæcum and of a portion of the small intestine adjoining. Sections were made and examined microscopically, but they showed nothing which would account for the reserve prostration. Cultures from

the intestine were negative. However, the organism was recovered from a stool passed three days after feeding the bacterial suspension.

After the organism had been grown for one month its pathogenicity was again tested. Comparatively large doses failed to kill either guinea pigs or rabbits. It is evident from this that Bacillus "S" rapidly loses its pathogenicity. The original fatal dose was again obtained after passage through guinea pigs.

TOXICITY.

The filtrate from living cultures.—Two flasks, each containing 150 cubic centimeters of sterile bouillon, one being 1.5 per cent alkaline, the other two per cent acid, were inoculated and allowed to grow at 37° C. for twenty-four hours. The cultures were then each passed through a Berkefeld filter, and the filtrate injected in large and small amounts intraperitoneally into guinea pigs, and intravenously into rabbits. The result was negative. The cultures after growing for seven days in alkaline and acid bouillon respectively were filtered and the filtrate inoculated into rabbits and guinea pigs with negative results.

A search was then made for an endotoxin. Six complete slants of agar in tubes were inoculated and the organism allowed to grow twenty-four hours, it was then suspended in salt solution and placed in a shaking machine for eighteen hours. The filtrate was injected into guinea pigs and rabbits, without result.

Suspension of killed cultures.—Suspension of 24-hour growths of the bacilli were placed in an incubator at 60° C. for one hour, and plates were then made demonstrating the sterility of the suspension. Two guinea pigs were inoculated each with 2 cubic centimeters of the suspension; one rabbit received 2 cubic centimeters intravenously. After twenty-four hours the guinea pigs were both dead, the rabbit still alive. At autopsy it was demonstrated that the peritoneal cavity of each guinea pig contained a large amount of sero-purulent fluid. However, smears and cultures from this were negative. At the end of forty-eight hours the plates made from the killed suspension were examined. They were sterile.

Agglutination tests.—As all four cases occurred in private practice it was not possible to obtain blood from each patient. Blood in very small amount was obtained from Case I on a slide, and although accurate quantitative tests could not be made, those which were conducted were very suggestive.

The blood from Case I was diluted with salt solution 1 to 50 and hanging drop preparations made with controls in each case. Table III shows the result.

TABLE III.—*Serum from Case I.*

Organism.	Agglutination.
Case I, *Bacillus "S"*	+
Case II, *Bacillus "S"*	+
Case III, *Bacillus "S"*	+
Bacillus typhosus	—
Bacillus dysenteriæ	—
Bacillus coli	—

One rabbit (number 3227) was rendered immune to the original *Bacillus "S"* and another (number 3229) to *Bacillus "S"* isolated from Case II. Living cultures were used and inoculated intravenously in increasing doses. Tests were made constantly and the agglutinative limit was reached in six weeks, each rabbit was then bled and agglutination reactions made as shown in Tables IV and V.

TABLE IV.—*Serum from rabbit immunized to Bacillus "S" (Case I) incubated at 37° C. for three hours.*

Bacillus.	1–50.	1–100.	1–200.	1–400.	1–800.	1–1,600.	1–3,200.	1–6,400.	1–12,800.	1–25,600.
"S"	+	+ +	+ +	+	+ + +	+ + +	+	+	+?	—
"L"	+	+	+ +	+ +	—	+ +	+ +	+	+	—
"T"	+?	+	+	+ +	+	+ +	+	+	+?	—
Coli	—	—	—	—	—	—	—	—	—	—
Dysenteriæ	—	—	—	—	—	—	—	—	—	—
Typhi	—	—	—	—	—	—	—	—	—	—

TABLE V.—*Serum of rabbit immunized to Bacillus "S" (Case II) incubated at 37° C. for three hours.*

Bacillus.	1–50.	1–100.	1–200.	1–400.	1–800.	1–1,600.	1–3,200.	1–6,400.	1–12,800.	1–25,600.
"L"	+ +	+ +	+ + +	+ + +	+ +	+ +	+	+	+	+
"S"	+	+	+ +	+ +	+ +	+	+	+	+	+?
"T"	+	+	+	+ +	+	+	+	+	+	—
Coli	—	—	—	—	—	—	—	—	—	
Dysenteriæ	—	—	—	—	—	—	—	—		
Typhi	—	—	—	—	—	—	—	—	—	

All the tests were made macroscopically, test tubes containing suspensions of the organism in normal salt solution being used. After each dilution was made, all were placed in the incubator at 37° C. for three hours before being examined. Controls were made in each case. The seemingly absolute specificity of the serum from each rabbit for the three organisms isolated is very striking, Shiga, colon, and typhoid bacilli being

unaffected in either case. Examination at the end of eighteen hours revealed absolutely no change in the homogeneity of the suspensions of the latter organism.

Summary.—During the past summer, especially during the months of July and August, several severe cases of infantile dysentery developed in Manila. A bacillus was isolated which culturally and morphologically resembled in some ways *B. dysenteriæ*, in others *B. coli* and *B. typhosus*. The specific agglutinins developed in animals through inoculation of this bacillus did not react with *B. dysenteriæ, B. coli* and *B. typhosus*, but organisms isolated from three other cases of dysentery were agglutinated in high dilutions, each by the specific serum of the other.

Serum from one patient agglutinated the bacillus isolated from the same patient, yet did not agglutinate other organisms from the same source.

Conclusions.—Intestinal organisms, especially the Shiga bacillus, exhibit such varied cultural and agglutinative characters when growing under different conditions and in different localities, that it is very difficult to classify them. From the above observations and a search through the literature we are led to believe that the bacillus isolated from these cases has hitherto not been described as one of the exciting factors in dysentery, but the specific character of the serum of one these cases and of that from rabbits immunized against *Bacillus "S"* seems to show conclusively that this bacillus was the cause of the epidemic of infantile dysentery which has been described.

PLAGUE PROCEDURE IN HONGKONG.

By Dr. J. M. Atkinson.[1]
(*Principal Civil Medical Officer Hongkong.*)

The plague procedure now in force in the colony of Victoria is as follows: 1. Notification. 2. Isolation. 3. Disinfection. 4. Segregation of contacts. 5. Cleansing operations.

1. *Notification.*—The main difficulty has been that the Chinese will not notify the authorities of the occurrence of the disease, preferring to hide their cases, and to deposit the body in the street after death. This procedure applies also to persons dying from other infectious diseases, such as smallpox, diphtheria, etc., and it is to a great extent caused by the dread these people have of disinfecting operations. This is proved by the fact that the percentage of bodies so deposited increased very considerably after the enforcement, in 1903, of the disinfection of houses on either side of the ones in which plague-infected rats had been found, in accordance with the recommendations made by Professor Simpson. The percentage of bodies so found was 32.7 in 1903 as compared with 25.1 in 1898.

2. *Isolation.*—Victims attacked by the disease are treated in the infectious disease hospitals at Kennedy Turn, one of which is a Government institution conducted as such institutions are in the Occident, the other, a native branch of Tung Wah Hospital, administrated by the Chinese, but under our sanitary supervision.

District plague hospitals have been established in Victoria and Hongkong during the past two years in order to obviate the necessity of removing the patients to such a distance as the situation of the Kennedy Turn hospitals; they are also allowed to be treated by their own doctors, the intention being, by these concessions, to obtain the coöperation of the Chinese and to prevent or minimize the depositing of plague bodies in the streets.

3. *Disinfection.*—This is rigidly enforced, compensation being given for any damage done to clothing. The process of disinfection consists

[1] Read at the Fourth Annual Meeting of the Philippine Islands Medical Association, March 3, 1907.

in the removal of all bedding, clothing, curtains, mats, etc., to the disinfecting station, these articles being tied up into bundles with large sheets of calico and then put into baskets which are carried by coolies, government clothing being supplied temporarily to replace the personal garments of the occupants of the infected houses. The walls and floors of the house are then sprayed with a 1–1,000 solution of corrosive sublimate, the floors are scrubbed with a 5 per cent solution of Jeyes's fluid, the drains are flushed, all rat runs are opened and crude carbolic acid poured into them, afterwards they are filled with broken glass and stopped with cement.

4. *Segregation of contacts.*—At the beginning of an outbreak the infected premises are evacuated and the residents kept under medical supervision for twelve days in blocks of houses rented for the purpose of accommodating them, they being allowed to carry on their usual vocations during this period.

5. *Cleansing operations.*—In the spring of 1903, the governor, Sir H. A. Blake, S. C. M. G., decided if possible to obtain the coöperation of the Chinese in the work of sanitation. He took over a district in the most plague-stricken portion of the city and endeavored to show what could be done by a thorough cleansing of houses and clothing by the people themselves. The work was begun in the winter of 1903–4 and as a practical result we have been able to obtain the coöperation of the Chinese in the "cleansing operations" and now every winter a general cleansing of the houses is effected by these people. Hot water in portable boilers, soft soap and Jeyes's fluid are supplied, the sanitary department removing all the rubbish and refuse from the houses. The procedure is as follows: Each householder receives a notice in writing stating that in two days' time a visit of inspection will be paid by the sanitary inspector and if the premises are found to be dirty, they will be cleaned by the sanitary authorities. These notices are sent seriatim to the different houses, beginning with each health district simultaneously. In very few instances has it been found necessary to enforce government cleaning.

Cleanliness is undoubtedly the bed rock of sanitation, and to insure it both of persons and houses, the coöperation of the people must be secured, this aid being more especially necessary when we deal with an alien race, such as the Chinese.

It is an almost hopeless task to expect to stamp out plague entirely in Hongkong, because we are, owing to our geographical position, constantly exposed to reinfection from the neighboring countries, the disease being practically endemic in Canton, Swatow and Amoy. Many insanitary areas and buildings have been allowed to be erected, and it is only by their reërection on improved plans and by the rigid prevention of overcrowding that plague, or any other infectious disease can be eliminated

from Hongkong. This rebuilding will of necessity be a slow process, but it is being steadily effected by means of the new public health and building ordinance and by the government each year resuming some of the most insanitary areas of the town.

PLAGUE PROCEDURE, 1904.

The following rules have been adopted and carried out:

1. On finding a suspicious case of plague, notify the medical officer of health at once.

2. Removals of sick must be to the district hospitals when they are established, or to the existing hospitals, as may be decided by the medical officer.

3. When a guard is required, the police must be applied to, the district watchmen's committee being unable to arrange for the employment of district watchmen. Further, when anyone reports a case of sickness or a death in a house voluntarily, the guard, pending the diagnosis of the case, may be dispensed with, provided that the occupants of the infected floor are willing to give their clothes up for disinfection at once. In such a case the tenants of the infected floor will be free to go where they like after giving up their clothing, and if the case should be returned as one of plague, the disinfection of the floor can then be proceeded with.

4. On receiving confirmation of the suspicion of plague in a house, proceed without delay to the house with the necessary assistance and equipment, and disinfect.

5. The disinfecting operations are to be confined to the floor in which the case occurred, unless there is reason to believe that the sick person frequented other floors.

6. The whole of the house should, however, be cleansed and the tenants of the noninfected floors may do this themselves if they are willing. Disinfecting fluid (Jeyes's) to be given for that purpose.

7. In cases where it is considered necessary to pull down ceilings, etc., in other than infected floors, the tenants may, if they wish, assist by first removing their furniture and afterwards clearing away the débris; but the board's officers must see that the débris is properly sprayed before removal, so as to lay the dust, and that the débris is put into the dust carts and not made use of by the people. The joints, etc., bared by such removal of ceiling or linings should also be sprayed.

8. The cleansing and disinfection of the infected floor must be wholly done by the board's officers.

9. People turned out of houses on account of plague must always be offered shelter in the block of houses rented by the board for this purpose, and help in the removal of their effects to such shelters must be offered.

10. The disinfecting operations are to be done in the manner and order laid down in the attached directions:

DISINFECTION OF INFECTED PREMISES.

This is carried out by a European officer assisted by eight colored foremen, a Chinese foreman, and a varying number of coolies. As soon as it is known that a case of the disease has occurred at any house, a Chinese constable is sent from the nearest police station to detain all persons found therein (By-law 22, Ordinance 15 of 1894), and the officer in charge of the disinfection proceeds to the house to ascertain how many persons are detained there. He then procures, either from the matshed at Praya East or from the disinfecting station, as many suits of government clothing as are needed for the persons so detained, and having thus provided these persons with clothing, he removes their own clothing, bedding, curtains and carpets to the steam disinfecting station, the clothing being tied up in sheets dipped in a solution of Jeyes's fluid and conveyed through the streets in baskets; persons who are able to obtain new or clean clothing from some uninfected premises are, however, not detained after they have discarded their infected clothing and have handed it to the inspector for disinfection. New goods, silk clothing which has not been recently worn, furs and leather goods are not removed to the steam disinfector, but must as a general rule remain on the premises until they have been fumigated. When the clothing, etc., is returned (in the course of some two hours) from the disinfecting station, the persons who have been detained are required to put on their own clothing and must then leave the premises for some five or six hours while the dwelling is disinfected and cleansed. The government clothing is returned to the disinfecting station to be steamed before it is again used. The people so displaced from their homes are at liberty to make use of the board's matshed shelters until the processes of disinfection of the premises are complete.

The disinfection of the premises consists in the spraying of the walls with a solution of bichloride of mercury (1 in 1,000) or fumigation with free chlorine obtained by the addition of diluted sulphuric acid to chlorinated lime (1 quart of a 1 to 8 solution of the acid to each pound of the chlorinated lime). Floors and furniture are scrubbed with a solution of Jeyes's fluid and the walls are then lime-washed, chlorinated lime being added to the lime wash in the proportion of one-half pound to the gallon.

PLAGUE MEASURES, 1906–7.

There are at present four plague inspectors for the city of Victoria, and one for Kowloon. There are eleven colored foreman interpreters, one for each district of the city of Victoria and one for Kowloon, who supervise the work of the rat catchers, assist in the house-to-house cleaning, and act as interpreters to the inspectors where necessary. There

are five gangs in the city of Victoria each consisting of one Chinese foreman, one artisan and seven coolies. Two inspectors have each one and one-half gangs, and the other two have a gang each, while Kowloon also has a gang consisting of a Chinese foreman, two artisans and ten coolies.

During nonepidemic periods the whole of this staff is engaged in house-to-house cleaning work, about ten houses or thirty floors a day being dealt with. Each tenant receives three days' notice, in writing, requiring him throughly to cleanse his premises. On the day fixed, the gang attends in the street opposite the houses named and supplies hot water and soap solution to the tenants, it cleans out all empty floors, basements, etc., the tenants themselves cleansing their own premises without assistance from us. The refuse turned out during this operation is removed by the gang to the nearest dust boat. The soap solution is also used by the tenants for washing their bed-boards, etc., in the street or on the veranda.

When the cleansing work is completed by the tenants, the inspector visits every floor, accompanied by the foreman interpreter and some of the coolies with a bucket of disinfectant (liquid fuel) and some mops; this liquid is applied to the sides and corners of the floors, to the skirtings, around the partitions of the cubicles, and to the stairs, under the personal supervision of the inspector. At this visit, when the floors are clear of furniture, and other incumbrances, the inspector makes special note of the condition of the ground surfaces, the absence of gratings to drain-inlets and ventilators, and the presence of rat runs, and all these matters are dealt with by legal notice at once. The tenants are requested by notice, to permit their bedding and spare clothing to be steamed, in order to destroy fleas and other vermin and their ova, but heretofore in Victoria they have persistently refused to allow this to be done, even though compensation is offered for all articles damaged. Should a case of plague appear in a house, the floor on which the case occurs is disinfected by the plague staff, the walls being sprayed with corrosive sublimate, and the floor and bed boards washed with Jeyes's fluid (half a pint to the gallon); crude carbolic acid is poured into the rat runs, which are then filled up with cement; and the clothing and bedding is sent to the disinfecting station to be steamed. The remaining floors of the infected house are cleansed by the tenants in the same manner as in the house-to-house cleaning. Should there be any ceilings or stair linings in the infected house, these are removed and compensation is paid for them, if the case has been duly reported, while illegalities are dealt with by notice. The compensation in the case of Chinese is assessed separately by the kaifong of the districts and by the plague inspector, and the assessments are dealt with by a committee of the sanitary board. The kaifong are appointed by the Tung Wah hospital

for the city of Victoria, and in Kowloon by the inhabitants of Kowloon Point, Yaumati, and Hunghom, respectively.

Any spare time at the disposal of the plague inspectors is occupied in paying special visits to houses in which cases of plague have occurred in the previous season, so as to be sure that they are free of rat runs and provided with impervious ground surfaces.

The Chinese have established public dispensaries and also district plague hospitals, which in the city of Victoria are managed by a committee of which the registrar-general and the two Chinese members of the sanitary board are members; in Kowloon, a purely local committee manages the dispensary and the hospital. These institutions are supported by voluntary contributions, and each is in charge of a licenciate of the Hongkong College of Medicine for Chinese, who sees outpatients at the dispensary, performs vaccinations, visits patients in their own homes, and treats those in the district hospital. Notice of cases of infectious diseases are given by these doctors to the nearest district office, and in the case of plague, the patient may be treated in the district hospital.

FLEAS ENCOUNTERED IN HONGKONG.

In October last, seeing the importance attributed by the Indian Plague Commission to the agency of fleas in carrying the pest infection, I instructed Mr. Gilson, the colonial veterinary surgeon, and Dr. Heanley, the assistant bacteriologist, to report to me concerning the species of fleas and rats met with in Hongkong.

The varieties of fleas are as follows:

(a) *Ctenocephalus canis* Curtis.[2] This flea is found on cats and dogs, but it is frequently taken on man also. It is a small flea, variable in size and of a dark color. It is not so nocturnal in habits as the other fleas. Dr. Heanley and Mr. Gilson found it on *Mus decumanus* and on dogs and men.

(b) *Pulex cheopis* Rothschild or *pallidus* Tasch. This is the common rat flea and is met with on *Mus decumanus, Mus rattus* and the muskrat. It is small, light-colored and more or less nocturnal in its habits. In Hongkong it is found more frequently on *Mus decumanus.*

Normally, the rat flea (*P. cheopis* Rothsch.) is rarely found on man The insects will, however, attack guinea pigs and accordingly it would be advisible to set free some guinea pigs in a room where a case of plague has occurred. The infection of guinea pigs by *Pulex cheopis* Rothsch. has been proved, the same can not as yet be said concerning the infection of man by this species of *Pulex.* Satisfactory experimental proof of the power of any species of flea to communicate plague to man is at present wanting.

[2] For classification of fleas see *Proc. U. S. N. M.* (1905), **29**, 121–170.

(c) *Ceratophyllus fasciatus* Bosc. This is found on *Mus decumanus* and it is the common flea attacking the rat in Europe. It, like *Ctenocephalus canis* Curtis, has a comb of bristles behind the head and is thus distinguished from *P. cheopis* Rothsch.

(d) *Pulex irritans* Linn. or the human flea. This is small and light colored, being found exclusively in dark and dirty houses.

Some curious facts have developed in regard to fleas and their relation to plague. It is a fact that oilmen and dealers in oil never suffer from the infection. Not a single oilman was included among the million who died of plague in Egypt in 1897. Lingi of Pavia records that during twenty-seven years while he was attendant at the pesthouse in Smyrna, he found friction with oil more efficacious than any other medicine as a prophylactic against this disease. In this connection Capt. Ziston, I. M. S., states:

"Can the relative immunity of Calcutta and Madras compared with Bombay and the Punjab be due to the habit of daily anointing the body with oil in the two former presidencies?"

It is also notorious that in India visits at night to plague-infected houses have frequently been followed by fatal results, while the same dwellings could be entered with impunity during the day.

We are now waging war in Hongkong against fleas, the object being as far as possible to kill the ova. When the cleansing work is completed by the tenants, the inspector visits every floor, accompanied by the foreman interpreter and some of the coolies, with a bucket of *liquid fuel* (pesterine) and some mops, and this is applied to the sides and corners of the floors, and the skirtings and around the partitions of the cubicles. In other districts phenol is being used in the same away as a pulicide.

The tenants also are invited to have their bedding, clothing, etc., disinfected by steam. By these means it is hoped to destroy the fleas, and it will be interesting to see what effect these measures will have on incidence of plague this year in Hongkong.

During the dry winter season fleas are remarkably scarce, therefore, this investigation will be continued during the hot, damp months.

RATS ENCOUNTERED IN HONGKONG.

(a) *Mus rattus* Linn., the black or ship rat. The most common color of this animal is a dirty gray. The tail is longer than the head and body together, is generally slender and tapers to a fine point. The ears are moderately large, standing up distinct out of the fur and extending to the eye and even beyond it when laid forward. The animal frequents roofs of houses and even trees.

(b) *Mus decumanus* Pallas., the brown rat, also called the Norway or domestic rat. It is a large rat which in European countries has

gradually displaced *Mus rattus*. It is a burrowing animal and frequents drains and cellars. There is a little to choose in color between this and the black variety. The brown rat is grayer and of a lighter shade, and this color is more noticeable when a number of the two species are examined together. The tail is shorter than the head and body together, and ends in a blunt point. The ears are short.

(c) *Mus musculus* Linn., the common mouse. This resembles *M. rattus* rather than *M. decumanus*.

(d) *Sorex giganteus* Is. Geoffr., the musk rat or musk shrew. This is neither a rat proper nor a rodent, but belongs to the insectivora. Its outline closely resembles that of a rat, but it is appreciably smaller than *M. rattus*. It is distinguished by its overpowering, musky odor.

There are also hybrid varieties, presenting the long ears of *Mus rattus* and the short, coarse tail of *decumanus*, the typical characteristics of the different species being only attained by the adult male.

The following roughly gives the percentages of the different species of rats met with in Hongkong:-

	Per cent.
Black rats, *Mus rattus*	12
Brown rats, *Mus decumanus*	18
Mice, *Mus musculus*	48
Sorex giganteus	2
Hybrid rats, size of *M. rattus*	5
Undetermined rats	15

TABLE I.—*Showing the number of cases of plague known to have occurred in the colony each month from 1895 to 1904.*

Month.	1895.	1896.	1897.	1898.	1899.	1900.	1901.	1902.	1903.	1904.
January	------	49	------	9	1	8	7	1	4	------
February	------	125	------	67	2	8	14	1	29	3
March	------	168	------	137	25	5	54	2	115	4
April	3	316	------	468	101	94	160	27	272	40
May	2	344	8	534	421	326	701	157	515	135
June	13	118	1	92	514	325	551	194	343	194
July	2	52	11	7	263	209	109	131	85	96
August	4	25	1	2	86	80	27	50	32	19
September	3	9	1	1	57	16	24	2	9	9
October	------	2	------	2	4	12	1	2	5	Nil.
November	5	1	2	------	1	2	1	1	4	5
December	12	------	2	1	11	2	2	4	2	5
Total	44	1,204	21	1,320	1,486	1,087	1,651	572	1,415	510

AN INVESTIGATION OF THE QUANTITATIVE RELATIONSHIPS BETWEEN AGGLUTININ, AGGLUTINOID AND AGGLUTINABLE SUBSTANCE.

By Y. K. Ohno.[1]

(From the Serum Division, Biological Laboratory, Bureau of Science, Manila, P. I.)

This article is a summary of an extensive piece of experimental work conducted for the last two years as a continuation of previous studies entitled "Equation of Curves and the Agglutination Phenomenon" (read before the Annual Meeting of the Association for Medical Research, March 24, 1905), and "The Relation between Agglutinin and Bacteriolysin" (read before the Section of Bacteriology, Hygiene and Infectious Diseases, Japanese Medical Congress, Tokyo, March 4, 1906). After numerous preliminary studies the attempt was made to determine the law governing the mechanism of agglutination by the employment of physico-chemical methods, and formulæ were established which expressed with exactness the quantitative reactions occurring between agglutinin, agglutinoid and agglutinable substance.

The preliminary studies established an exact technique. A bacterial suspension was used of which the dose constantly employed, (0.5 cubic centimeter) contained 0.5 milligram of bacteria by weight. Each test tube in every experiment contained a constant volume of 2 cubic centimeters.[2] The bacterial emulsion was made from 24-hour agar slant cultures killed by the addition of 1 per cent formalin. It was found that the dead cultures registered more exactly the limits of agglutination than living ones. The experiments were performed with *B. typhosus, B. dysenteriæ, B. paratyphosus, B. coli, B. pyocyaneus, V. choleræ, Meningococcus intracellularis,* and *Staphylococcus pyogenes aureus,* together with corresponding immune sera. In performing the agglutination experiments the various dilutions were prepared, placed in the incubator at 37° C. and allowed to stand for twenty-four hours. The

[1] Read at the Fourth Annual Meeting of the Philippine Islands Medical Association at Manila, P. I., on March 2, 1907.

[2] Which each test tube contains 0.5 milligram of bacteria.

macroscopic method was uniformly employed. Each one of the procedures mentioned above was adopted after critical study and experimentation and further studies were made to ascertain the optimum quantity and concentration of salt solution.

In standardizing the units, a unit of agglutinin (or agglutinoid) was selected as that amount which is contained in a quantity of serum sufficient to agglutinate completely 1 milligram of bacterial culture suspended in 0.85 per cent salt solution when the experiment is conducted for twenty-four hours at 37° C. Complete agglutination was defined as that reaction which results in sedimentation of all particles with clearing of the fluid. For the purposes of experiment it is assumed that one unit of agglutinin will always combine with a certain fixed amount of agglutinable substance. Having established a definite and exact technique by these studies and having critically reviewed similar studies of Joos, Eisenberg and Folk and others, experiments follow which are used in the elaboration of formulæ representing the values of agglutinin A and agglutinoid B in 1 cubic centimeter of agglutinating serum. The formulæ established are as follows:

$$A = \frac{CM\,(G - m)}{M - m}$$

$$B = \frac{Cm\,(M - G)}{M - m}$$

$$\frac{1}{X} = \frac{G - m}{M - m}$$

In these equations:

A = the number of agglutinin units (Ag) contained in 1 cubic centimeter of serum tested.

B = the number of agglutinoid units (Ao) contained in 1 cubic centimeter of serum.

C = the weight in milligrams of the agglutinable substance contained in each tube, namely the weight contained in 0.5 milligram of bacteria.

$\frac{1}{G}$ = the highest serum dilution in which complete agglutination occurs.

$\frac{1}{m}$ = the serum dilution just too low to cause a visible agglutination but still causing invisible agglutination.

$\frac{1}{M}$ = the serum dilution just too high to cause visible agglutination but still causing invisible agglutination.

$\frac{C}{X}$ = the quantity of substance agglutinated at a serum dilution of $\frac{1}{m}$ or $\frac{1}{M}$.

The correctness of the above equations was established by proving through them the following propositions:

1. The value of X must always be the same with the same bacterial culture, notwithstanding all modifications which may occur in the serum.

2. The value of A and of B must be constant or nearly so, even if we vary the value of C within limits which do not cause X to change.[3]

3. The quantity of bacterial culture uniting with agglutinin at any particular degree of reaction can be established and remains about the same, when we use the same bacterial suspension, notwithstanding all modifications which may occur in the serum.

4. Having determined the quantities of bacterial culture uniting with agglutinin in the different grades of reaction, the value of "m" can be calculated from the known amount of agglutinated substance concerned in the antephase of $\frac{1}{D}$ dilution of the serum.[4]

5. In the same way the value of M can be calculated from the known value of agglutinated substance concerned in the postphase at $\frac{1}{D}$ dilution of the serum.

6. The value of G can be calculated from the known value of agglutinated substance at $\frac{1}{D}$ dilution in the antephase of $\frac{1}{M}$.

The failure of other investigators in their attempts to find the law governing the agglutination phenomena and to express it in a mathematical equation, proceeds in part either from their selection of standards of measurement which are not sufficiently accurate, or from their adoption of unsuitable units, or, as in the cases of Eisenberg and Volk and Craw and Joos, from their allowing too short a time for complete agglutination to occur. The preliminary steps which led to my discovering the formula for agglutination were, first, my assumption that agglutinin, agglutinoid and agglutinable substance always unite according to a fixed ratio; second my adoption of suitable units; third, my adoption of a scale expressing the degrees of agglutination with a fair degree of accuracy; fourth, my assumption that agglutinoid is present to some extent in every agglutinating serum; and fifth, my assumption that every reaction of agglutination is accompanied by a certain amount of invisible agglutination.

As the result of their studies, Eisenberg and Volk insist that the combining ratio of agglutinin and agglutinable substance varies according to the quantities employed and they express this fact by means of their "coëfficient of absorption." My investigations lead to the conclusion that these experimentors have three constant errors in their experiments, first, their neglect of agglutinoid; second, *their failure to take into account the degeneration of agglutinin, produced by the temperature during the agglutination test;* and third, *their failure to appreciate the difference between the quantity of united (fixed) agglutinin and that of agglutinated agglutinin.*

[3] If the value of C is too high or too low, the density of the bacterial emulsion in the test tube is so much changed that it is not possible to determine exactly the point represented by $\frac{C}{X}$.

[4] $\frac{1}{D}$ = the degree of dilution of the agglutinating serum in any one given test tube.

In the antephase of agglutination, the serum, even though it contain a great quantity of agglutinin, can agglutinate only that quantity of agglutinable substance which is not picked up by agglutinoid, as the latter unites more readily than agglutinin with agglutinable substance; therefore, the proportions of agglutinin uniting with agglutinable substance during the antephase do not show the usual regular proportions. However, the regular ratio between agglutinoid and agglutinable substance can be shown by subtracting the available agglutinable substance, as indicated by the degree of agglutination, from the amount of agglutinable substance introduced into the test tube. The variations in the quantity of agglutinable substance united with agglutinin at different serum dilutions is, therefore, not a proof of different grades of absorption as Eisenberg and Volk consider it to be, but is dependent upon the presence of agglutinoid.

The rate of conversion of agglutinin to agglutinoid varies with the temperature and the dilution at which the agglutination test is performed, being greater at a high temperature and in high dilution. Eisenberg and Volk did not pay attention to this fact, although it is of importance in considering a theory of agglutination.

I accept the view first advanced by Bordet that agglutination may be divided into a stage of fixation of agglutinin by bacilli, and a stage of aggregation of bacilli united with agglutinin. However, according to the results of my experiments, three and one-half to four and one-half hours at 37° C. or four and one-half to five and one-half hours at room temperature (first two hours at 37° C.) is necessary for the fixation of agglutinin to bacilli. The time required for aggregation is much longer than that needed for fixation, and if we do not allow sufficient time for aggregation to affect all the quantity of fixed agglutinable substance, we will not be able to form an accurate idea of the degree of agglutination produced by any given amount of serum. My experiments indicate that it requires the time limits given above for a complete union and from twenty to twenty-four hours at 37° C. for complete aggregation. As Eisenberg and Volk conducted their tests for only two hours at 37° C. followed by twenty-two hours at room temperature, I estimate that they recognized only three-fifths of the real value of their serum; therefore, the quantity of absorbed agglutinin, calculated by Eisenberg and Volk, is larger than the real quantity by a certain amount of agglutinin and agglutinoid, which is to be given by the expression:

$$(\tfrac{3}{2}\, r' + d')\ \mathrm{AgE} - \mathrm{AgD}$$

Where r'=the quantity of agglutinin remaining ununited;
d'=number of units of agglutinin degenerating during the test; and AgE and AgD represent respectively the agglutinin and agglutinoid units of Eisenberg and Volk.

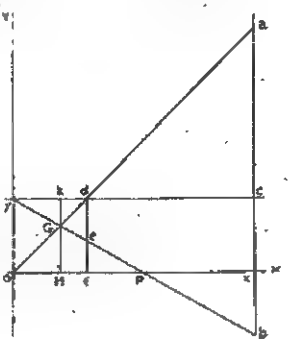
From this equation we observe a third source of error in Eisenberg and Volk's method of obtaining their "coefficient of absorption."

After correcting the errors just pointed out, a repetition of the experiments performed according to the method of Eisenberg and Volk gives values agreeing entirely with those calculated and this also substantiates the truth of my assumptions and formulæ.

The curves graphically representing the phenomenon of agglutination (see fig. 1) are two straight lines ($x - y = 0$ and $\frac{B}{A}x + y - C = 0$) which interact with each other and fulfill the equation.

$$Bx^2 + Axy - ACx + ACy - Bxy - Ay^2 = 0$$

where x is the function of the quantity of serum and y that of the degree of agglutination (that is, the quantity of agglutinable substance agglutinated) within the limits of $x = \frac{AC}{B}$ and $y = \frac{AB}{A+B}$, i. e., within the limits of the agglutinative power of a serum which contains A of agglutinin unit (Ag) and B of agglutinoid unit (Ao) in 1 cubic centimeter, C being the quantity of bacterial culture in each test tube.



$Ox = ax = A$
$Oy = cx = C$
$bx + ax = B$
The equation for the curve O. G P is $Bx^2 + Axy - ACx + ACy - Bxy - Ay^2 = 0$
FIG. 1

The serum is also represented by a straight line ao (see fig. 2) the formula of which is $y = \frac{B}{A}x$. The limit of agglutination is ωa, ω being the center of coördinates and a having an ordinate $\frac{1}{2}$ Ao (agglutinoid unit), while at the point e which has an abscissa $\frac{1}{2}\left(\frac{A}{A+B}\right)$ the phenomenon is most complete. The limit of the quantity of agglutinoid which causes the disappearance of agglutination (in the macroscopical test) is A $(X - 1)$, where the value of X varies according to the kind of bacilli, while the relation between the quantities of agglutinin and agglutinoid required to keep complete agglutination with some degree of serum dilution, while both substances are variable, is $\frac{A}{B} > \frac{f}{C-f}$, where f is the quantity of agglutinated agglutinable substance which varies according to the different species of bacilli.

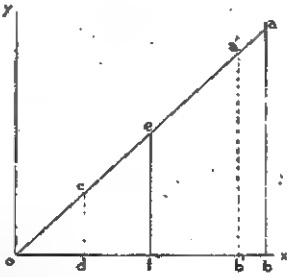


FIG. 2.

Serum has a coefficient of viscosity about 300 times greater than that

of salt solution. This great viscosity causes the depression of the phenomena of agglutination. The grade of depression, plotted in the coördinate system, is approximately expressed by the formula,

$$y^2 = 4\,Kx.$$

the equation of a parabolic curve, where y is the degree of depression; x the quantity of serum in the test tube, and K is a constant, which varies according to the type of serum as follows:

K	with the serum of
206.5	rabbit
233.5	calf
345.8	horse
367.0	cow

where $y=100$ (to express the percentage of depression of agglutination with a certain quantity of united agglutinin) and $x=1$ (taking 2 cubic centimeters of serum in a test tube as the unit). In consideration of this fact, it seems that we need to correct the values of agglutinin and agglutinoid from the formula

$$A = CM\,\frac{G - m}{M - m}$$

$$B = Cm\,\frac{M - G}{M - m}$$

because the value of m is somewhat smaller than it should be, but practically we need not make such a correction because the difference is so very slight that we can neglect it in calculation, it (δ) being expressed by the equation

$$\delta = \frac{1}{50}\sqrt{KD}$$

where D is the reciprocal of serum dilution $\frac{1}{D}$, while the value of K varies from 14 to 20. Therefore, the value of δ is approximately 0.84, at the maximum, when M=10. When M=10,000 the value of δ is 0.004 and so on. In estimating the *grade of agglutination,* on the other hand, we must correct by adding the difference, because this quantity is greatly influenced by even such a slight amount. When we correct the quantity of united agglutinin by adding the difference, we obtain agreement between the calculated grades of agglutination *in both ante- and post-phase,* in cases in which the same quantity of agglutinin is united and this supports the theory that agglutinin always combines with agglutinable substance in a constant ratio and demonstrates the influence of serum viscosity upon agglutination.

While at the post-phase of agglutination the total quantity of agglutinin is absorbed (united) by the agglutinable substance, during the

antephase only those units of agglutinable substance which remain united with agglutinoid can absorb equal units of agglutinin; that is:

$$\text{"quantity of combined agglutinin"} = C\ (\text{units of agglutinable substance}) - \frac{B}{D}$$

while

$$\text{"quantity of free remaining agglutinin"} = \frac{A}{D} - \text{"quantity of combined agglutinin"}$$

$$= \frac{A}{D} - \left(C - \frac{B}{D}\right)$$

where $\frac{1}{D}$ is the grade of dilution and $\frac{B}{D}$ must be within the limits of $C = \frac{B}{D}$. From these equations it needs no proof that Arrhenius' formula is not correct, because according to his formula:

$$\frac{(\text{quantity of absorbed agglutinin})^2}{(\text{quantity of free-remained agglutinin})^2} = k$$

that is:

$$\frac{\left(C - \frac{B}{D}\right)^2}{\left(\frac{A}{D} - C + \frac{B}{D}\right)^2} = k^1$$

which is impossible *when D and C are variable,* even with any values of C and D.

The degeneration of one unit of agglutinin will not always lead to the production of one unit of agglutinoid. In many cases the agglutinin degenerates even more completely, the uniting group being destroyed as well as the functioning group. Thus the conversion of agglutinin into agglutinoid is irregular both in regard to rate and amount. The destruction of agglutinophore groups is greater on the addition of alkali than of acid, while formalin does not affect the serum so seriously. From the results of my experiments we see that the irregular production of agglutinoid by the degeneration of agglutinin is not due to a difference between the haptophore groups of agglutinin and agglutinoid, but to the degree of destruction of the haptophorous groups of agglutinin, brought about by chemical or physical factors. We also secure a similar irregularity in the production of agglutinoid in the blood of animals.

The results of experiments show us that the quantity of agglutinoid production is not in a constant ratio to the degeneration of agglutinin. The cause is to be found in the irregularity of agglutinin production and in some forces which are able to destroy not only hemiagglutinin, but also haptophore groups.

If a serum contains two different kinds of agglutinin A and A′, and their respective agglutinoids B and B′, the haptophore groups of A and

B being entirely distinct from that of A′ and B′, and if the quantities of A and A′ and also those of B and B′ are not equal, then the curve graphically representing the agglutination phenomena of such a serum is composed of four straight lines intersecting at three points and having two apices like a mountain with two peaks. Such a serum can be termed "poly-apical," in contradistinction to one having only one apex, which would consequently be called a "mono-apex-serum." With the former it is difficult to estimate the value of agglutinin and agglutinoid from the formula

$$A = CM\frac{G - m}{M - m}$$

$$B = Cm\frac{M - G}{M - m}.$$

with known values of m, G, and M, because there are two factors for G. For this reason *I have used only mono-apex-serum, either obtained as such directly from animals or man or by a modification of a poly-apical variety.* It is very interesting to discuss the character of poly-apical sera, but their consideration depends rather upon the relations between the bacterial receptors and amboceptors, and consequently I will leave this topic for another paper which will be especially devoted to this problem.

At the result of this series of experiments I am of the opinion that the union of agglutinin and agglutinable substance is not analogous to the fixation of dye by a tissue, as Bordet considers it to be, but I believe it to be a chemical reaction, as is maintained by Ehrlich.

The detailed report, of which this is a summary, will shortly be published in another journal.

PECULIAR CASES OF TRAUMATISM OF INTERNAL ORGANS, SOME DUE TO TROPICAL CONDITIONS AND PRACTICES.

By MAXIMILIAN HERZOG.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

During the years 1904 and 1905, I encountered among my autopsy material five cases of fatal traumatism of internal organs without external injuries. However, in two of these five instances fractured ribs were responsible for the interpal damage, which was followed by fatal hæmorrhage. Each one of the five presents quite peculiar and noteworthy features, two are probably unique in kind; two were of rupture of the spleen occurring in splenomegaly, two of rupure of the heart, one a fatty heart which, in the absense of any other injury, was pierced by a rib in consequence of a slight fall, and one case, rupture of fatty liver, occurred during parturition because of native obstetrical practice.

TWO CASES OF SPLEEN RUPTURE IN SPLENOMEGALY.

Rupture of the spleen in the tropics is probably not at all rare, although heretofore, it appears to have been the general impression that it is so.

Glogner[1] has quite recently called attention to its occurrence in Java, where, during the years 1893 to 1898 he saw ten cases of rupture of the spleen. A summary of Glogner's observations will be of interest. In all ten cases, the spleen was enlarged, in several instances very much so; in all, the cause of the rupture, followed by fatal hæmorrhage, was comparatively slight; in four cases malarial parasites were found in the spleen upon post-mortem examination. Glogner, from his observations, draws the practical conclusion that a person during or after a malarial infection, as long as an enlarged spleen is present, should be guarded carefully against any danger which might lead to a rupture of the spleen.

Our own two cases of rupture of the spleen are the following:

CASE I.—J. R., a 15-year old, male, Filipino boy, on July 15, 1904, was brought to the San Juan de Dios Hospital. It appears that the boy had received a slight kick or had suffered a fall. No diagnosis was made and he died syncope on July 16, in the afternoon.

[1] Glogner: Ueber Milzrupturen in den Tropen. *Arch. f. Schiffs u. Trop. Hyg.* (1906), 10, 17.

Necropsy (*No. 1003*).—Post-mortem examination made July 17, 1904, at 10 a. m., fifteen hours after death. Body of a well-developed young male native. Post-mortem rigidity still quite well marked. Post mortem lividity very moderate. The whole surface, particularly the mucous membranes, is very pale and anæmic. The abdomen appears much distended, particularly the upper part. There are no signs of external violence, and no wounds or abrasions. On opening the abdomen very extensive blood coagula are found to fill every available space below the diaphragm. Serum has collected in the dependent parts of the abdominal cavity, and the mass of serum and coagula removed amounts to about two to three liters. All the organs are found to be very anæmic. The heart is soft and flabby, but otherwise normal. The lungs are rather collapsed and pale pink in color. Both of them have formed some adhesions and the apex of the right lung contains four caseous nodules, varying in size from a pea to a hazelnut. Otherwise, the lungs, the trachea, the bronchi and the larynx are normal. The spleen is very soft, flabby and friable, measuring 23 by 10 by 6½ centimeters and weighing 655 grams. The capsule is wrinkled, transparent and grayish-blue. The veins entering the hilum are very much enlarged and have very thin walls. On the posterior, lateral surface of the spleen—namely, that which was in contact with the internal thoracic wall of the left side—there is found a rupture, which extends from the outer lateral margin of the organ toward the hilum. The rupture is about 6 centimeters long and is directed somewhat downwards. It forms a triangular gap, the base of which is found at the hilum, being 2½ centimeters long. The rupture has torn into some of the larger branches of the splenic vein. The lesser omentum contains a small, round body of the size of a hazelnut, which is either an accessory spleen or a hæmolymph gland. On inspecting the internal wall of the thoracic cavity, it is found that the 9th rib of the left side is fractured. This fracture is situated 9.5 centimeters behind the anterior end of the rib. It is an incomplete, green-stick fracture, and is situated in the mid-axillary line. The anterior segment of the fracture is very sharply pointed. It projects somewhat into the pleura costalis. The region around this fracture, for a radius of several centimeters, is hæmorrhagic. It is clear that this fracture must have been produced by a dull force, which, however, left no sign on the integument; it was probably a force exerted very quickly, not crushing the soft parts, but splitting the rib and driving the anterior fragment into the exceedingly soft, friable, enlarged spleen and producing a rupture. The kidneys are normal. The adrenals are normal. The capsule of the liver is smooth and transparent, and in color pale pinkish-blue, the upper surface showing a number of small, punctiform hæmorrhages. On the cut surface the organ appears brownish-pink. The gall-bladder is normal. The ducts are normal. The mucosa of the duodenum and stomach is pale. The small intestine, the large intestine, the prostate, etc., are normal. The brain and cord are normal.

Anatomical diagnosis.—Splenomegaly (primary ?), fracture of the ninth rib of the left side, rupture of the spleen, hæmorrhage, general anæmia of all the internal organs, tuberculosis of the apex of the right lung. No malarial parasites were found in smears prepared from the spleen.

Case II.—M. V., 25 years old, was working on a new building on February 13, 1905. He was engaged in lifting, by means of a lever, certain heavy weights, and just as he had brought the lever to the required elevation, he staggered and fell to the ground. His friends applied "smelling salts," thinking that he had fainted, but as he did not respond to this treatment, the Bureau of Health was notified. The time between the injury and his death was probably about twenty minutes. His wife stated that his health had not varied since she had known him. The post-mortem examination (Necropsy No. 1108) was made two hours

after death. The findings were: Beginning cirrhosis of the liver, splenomegaly (very large spleen), rupture of the spleen, copious hæmorrhage into the abdominal cavity. No external injuries, no ribs fractured. Smears from the spleen showed neither malarial parasites nor the Donovan-Leishmann bodies.

PERFORATION OF THE HEART.

The two following descriptions refer to cases of perforation of the heart. In one of them the myocardium was ruptured by a fractured rib, *but not the pericardium* and the victim did not die from the effects of losing a large amount of blood, but from compression of the heart and cessation of its action. In the second case a floating rib perforated a heart which was in an advanced condition of fatty degeneration.

CASE III.—Necropsy No. 1004. Sra. M. R., Filipina, age, 25, died July 17, 1904. The post-mortem examination was made July 18, twelve hourse after death. Immediate cause of death not known. It was stated that she had been struck by a carromata shortly before she died. Body of a well-developed, young, native woman, 25 to 30 years of age. Post-mortem rigidity strongly marked. Post-mortem lividity quite noticeable. Abdomen somewhat distended. A repeated careful inspection fails to show any signs of external violence. No wounds, contusions or abrasions of any kind to be seen. On opening the thoracic cavity, the pericardium is found to be much distended, and shining through it there appears to be a firm, dark, blood coagulum. On opening the pericardium it is found to contain a large amount of dark, coagulated, gelatinous blood and blood-tinged serum, distending the pericardium *ad maximum* and compressing the heart. A careful examination fails to show any perforation in the pericardium. The heart, which weighs about 226 grams, presents a perforation, which begins 2 centimeters to the left of the anterior border of the interventricular septum. The perforation extends almost horizontally toward the left, being a little downwardly inclined. It forms a slit 2.2 centimeters long, running 5 centimeters above the apex and 5.5 centimeters below the sulcus of the heart. The edges of the perforation are almost clean-cut where they enter the myocardium, as if they had been produced by a dull, somewhat serrated knife. The cut takes a somewhat downward and inward course, traveling through the whole thickness of the myocardium. Where the cut enters the cavity of the heart, the margins are not very smooth, but rather irregular and ragged. The consistensy of the myocardium is good. Its color is pinkish-brown and all the serous surfaces are smooth. There are no atheromatous changes. The heart is covered with a very moderate amount of epicardial fat. In short, the whole organ is absolutely normal. After the removal of the lungs (the apex of the right one showing a very few tubercles and a little caseous nodule not larger than a lentil) it is seen that the second, fourth and fifth ribs are fractured. The fracture of the second rib is found to be 7.5 centimeters posterior to the sternal articulation, that of the fourth one 9 and that of the fifth one 9.5 centimeters. The anterior fragments are directed inwards. The fragments of the fourth and fifth ribs are very sharp and are surrounded by an area or subpleural blood extravasation. However, these fragments have not perforated the pleura costalis. The extravasated blood is strictly subpleural and no free blood is found on the surface on the pleura. The uterus appears somewhat enlarged and the left ovary shows a fresh, but already closed corpus lutem. On opening the uterine cavity, a little hæmorrhagic mass, about one-half centimeter in diameter, is found embedded in the mucosa of the posterior wall, near the entrance of the left tube.

All the organs of the body, with the exception of the apex of the right lung are found to be absolutely normal. They are all more or less congested with dark, fluid blood. It appears clear that the woman must have been struck at the side of her body or in the back by a swiftly moving force. This force, however, did not produce any signs of external violence, particularly no contusions, abrasions or wounds. The force traveled through the soft parts, and meeting the resistance of the ribs, fractured them. The anterior, sharp fragment of the fourth or of the fifth rib was evidently driven into the wall of the left ventricle, producing a complete perforation. A highly interesting point is that the sharp fragments neither perforated the pleura costalis nor the parietal layer of the pericardium.

Only when the resistance of the firm wall of the ventricle was encountered, did a rupture or perforation occur, a hæmorrhage taking place, and when the pericardium was completely filled and the myocardium much compressed, the heart's action came to a sudden standstill. Death occurred from syncope.

Anatomical diagnosis.—Fracture of the second, fourth and fifth ribs of the left side. Complete perforation of the wall of the left ventricle. Hæmorrhage into the pericardium. Compression of the myocardium. Beginning tuberculosis of the apex of the right lung.

Microscopic examination of the myocardium showed it to be perfectly normal.

Case IV.—Necropsy No. 1185, May 15, 1905. A. R., 70 years old, female Filipina, died May 13, 1905, at 3 p. m. Post-mortem examination forty-two hours after death. This woman fell downstairs. She immediately went into collapse and died within fifteen minutes after the accident.

Body of a medium-sized, quite fat woman, probably younger than 70 years old, perhaps 60. Post-mortem rigidity has disappeared, post-mortem lividity well marked and extensive over the dependent parts of the body. Putrefactive changes well advanced. A close inspection fails to show any signs of external violence; there are no signs of a contusion, the skin shows no areas of suggilation. On opening the body, the abdominal cavity presents nothing abnormal. However, in the thoracic cavity, the pericardium is found distended and it contains a soft blood coagulum and hæmorrhagic, dirty-brown fluid. A blood coagulum of the size of two fists is also found in the right pleural cavity. The anterior surface of the pericardium presents a slit 18 millimeters long. Its direction is from above downward, its margins are sharp cut, linear on the whole, but here and there irregular and wavy, however, not serrated or fringed. Corresponding to this slit in the pericardium there is a perforation in the anterior wall of the right ventricle. It is almost immediately to the right of the interventricular septum and 8.5 centimeters above the apex of the heart. It is 7 millimeters long but not clean cut, rather irregular and with ragged margins. Its direction is oblique, being from above and to the left, to below and to the right. The perforation traverses the whole of the myocardium which is here less than 2 millimeters thick. The exit of the perforation into the endocardium is about one-half the size of its entrance at the outer surface of the myocardium. The heart as a whole is somewhat enlarged in its diameters; it measures from base to apex 13.5 centimeters; 9 centimeters across the broadest point, and it is 7 centimeters thick. It weighs, including the arch of the aorta, 380 grams. The walls of the left ventricle are thickened, but the myocardium here, as elsewhere, is very friable, flabby and soft and of a grayish-yellowish, dirty-pink color; it is porous and honeycombed, but this condition is evidently due to the action of gas forming bacilli and must be looked upon as a post-mortem change. The right ventricle is dilated; its wall, particularly the anterior part, is very thin, measuring on an average only 2 to 3 millimeters in thickness. The endocardium is smooth, the valves show no change, but the right auriculo-ventricular opening is enlarged. The whole arch

of the aorta is atheromatous and the intima covered with calcareous patches; the coronaries are likewise atheromatous. The lungs are normal. The osseous framework of the thorax is normal, none of the ribs are broken, but both of the tenth ribs are unusually long and their free, floating ends reach very much forward. The tissues over the free end of the tenth rib of the right side are decidedly hypersemic, however, there is no break of continuity in this region. The spleen is very small, soft and mushy. The kidneys are small, slightly uneven, the capsules peel off with some difficulty. Other abdominal organs, normal; putrefactive changes well advanced. The brain is of medium size (weight, 1,210 grams), all the arteries at the base are in an advanced stage of atheromatosis.

Anatomical diagnosis.—Hypertrophy with concentric atrophy, fatty degeneration, and dilatation of the myocardium. Perforation of the myocardium and of the atrophic anterior wall of the right ventricle; hæmorrhage into the pericardium and into the left pleural cavity. Extensive atheromatosis of the aorta, of the coronary arteries and of all the vessels at the base of the brain. Atrophic interstitial nephritis of moderate degree. Abnormal lenght of both of the tenth ribs.

Epicrisis.—It is evident that in consequence of the fall, the free end of an unusually long tenth rib which reached far forward perforated the pericardium and the atrophic, degenerated myocardium, and this led to the hæmorrhage which became fatal inside of a short time after the accident had happened.

RUPTURE OF THE LIVER DUE TO AN OBSTETRICAL PRACTICE IN THE PHILIPPINE ISLANDS.

It is a well-known fact that certain races have adopted peculiar practices to assist a parturient woman during labor, in order to facilitate and hasten the expulsion of the child from the uterus. The North-American Indians, for instance, place a woman in labor with her back against a tree, an old woman then stands behind the tree, reaches around the latter as well as the woman propped up against it, and makes violent compression over her abdominal region. The native Filipinos have a method which, while different in arrangement, is based upon the same principle. They place a folded piece of cloth, a long towel, or some similar thing above the bony pelvis and around the loins of the woman in labor, and then one or two persons with all their might make traction on the encircling bandage. That this method may, under special circumstances, lead to much harm, in fact to a fatal issue, is shown by the following case. Nothing is known concerning its clinical history, except that one of the medical inspectors of the Bureau of Health was called in February, 1906, to view the remains of a woman who had died quite suddenly during labor. The body was sent to the morgue, where a post-mortem examination was made. The following were the findings:

CASE V.—Necropsy No. 1661, about twenty hours after death. C., age unknown, a female Filipina, died February 16, 1906, at 1.15 p. m. Cause of death, unknown. Body of a woman, about 35 years old, of medium size and fair nutrition. The woman appears to be pregnant, at or near full term. She appears to be a primipara because the abdominal wall does not present any striæ. There are no external anomalies, but the labium majorum of the left side shows a pediculated fibroma of the size and shape of a large pear. A piece of cloth

in the form of a bandage is tied around the upper part of the abdomen, above the umbilicus. This bandage has been drawn so tightly that it has left a deep, annular impression running around the abdomen and back. Post-mortem rigidity has almost disappeared. The post-mortem lividity is well advanced. On cutting through the skin, the tissues are found to be very anæmic and on cutting through the peritoneum the upper part of the abdominal cavity is found to be full of clotted and fluid blood. An examination shows that this hæmorrhage has come from a ruptured liver. Further examination of the internal organs shows the following: The heart is exceedingly soft and flabby, grayish-yellow in color. The spleen is small, soft and friable, otherwise normal. Both kidneys show signs of fatty and parenchymatous degeneration. The liver is large, somewhat swollen, weighs 2,280 grams, is pale-yellow in color, exceedingly soft and flabby and so friable that on handling it a rupture is produced on the upper surface of the left lobe. The upper surface of the right lobe presents two deep, lacerated perforations and the tissues here are suggilated with extravasated blood. It was at this place that clots of blood were found; on opening the abdomen, they needed to be removed in order to show the condition of the liver. Examination of the region of the liver and of the right thorax shows the ruptures in the liver to have been produced by the eleventh rib of the right side. It is possible that the outer one of the two perforations has been caused by the twelfth rib. The pleura over the external end of the eleventh rib shows a small area of blood extravasation. It is evident that when this rib was pressed against the liver, perforating the latter, there was enough force used to cause a slight hæmorrhage of the pleura over the end of this rib. The uterus contains a female child nine months old or, at least, near full term in breech presentation. The cervix is soft, somewhat hæmorrhagic and admits two fingers. Evidently, the first stage of labor had begun, but the membranes had not yet ruptured nor had detachment of the placenta taken place. The placenta itself is perfectly normal. All of the other organs including the brain are normal, but they are all profoundly anæmic. The eleventh and twelfth rib were removed and cleaned. The former, the outer end of which presented a sharp point, measured 135 centimeters in length, the latter 9 centimeters.

Microscopic examination of the various organs, pieces of which had been fixed in Zenker's solution and in osmic acid, shows the following: *Liver:* The protoplasm of the parenchyma cells is granular and finely vacuolated, the osmic acid preparations show numerous, small, disk-like, black granules and round, black granules, varying in size from a small coccus to about half the diameter of the cell nuclei. There are also seen black masses of the size of a liver or parenchyma cell and even larger, roundish bodies of this color; these are, of course, all the result of the profound fatty degeneration. The nuclei of the parenchyma cells are generally fairly well stained and many cells show two nuclei. The periportal, interlobular connective tissue shows a slight, but manifest, increase. The *renal* epithelium shows advanced cloudy swelling and fatty degeneration. In the spleen, marked changes are not present, and malarial parasites are not found. The *myocardial* fibers are very indistinctly striated, vacuolated and full of fat granules. The *fibroma of the vulva* is composed of loose, œdematous, fibrous connective tissue; it contains numerous, large vessels; this vascularity had probably developed during the period of gestation.

Anatomical diagnosis.—Fatty degeneration of the heart and of the kidneys and profound fatty degeneration of the liver; perforation of the latter by the eleventh rib, copious hæmorrhage, *uterus gravis menses X.*

The anatomical and histological examination of this case plainly shows that this woman was in the first stage of labor and that she was suffering from a profound fatty degeneration of the liver which may perhaps have been the first stage of acute, yellow atrophy of that organ. When the bandage was applied to assist in labor, as is habitually done among the natives, the force of the pressure was sufficiently great to drive the sharp point of the eleventh rib into a very soft, flabby, fatty liver, thus causing a rupture and fatal hæmorrhage.

THE HABITUAL USE OF OPIUM AS A FACTOR IN THE PRODUCTION OF DISEASES.

By Tee Han Kee.
(*From the Bureau of Health, Manila, P. I.*)[1]

It is not the intention of this paper to discuss at length the therapeutic use of opium as a medicine, nor is it my desire to treat of the symtomalogy and psychology of the opium habit, for such an attempt would lead away from by main purpose, which is to give an account of the motives of the Chinese in using opium; how they use it, and lastly what are the results, or, in other words, diseases produced by the habit.

Two main reasons could be given as the motives of the Chinese for using opium: 1. For pleasure. 2. As a medicine.

1. *For pleasure.*—After careful inquiry among the Chinese as to their reasons for using opium, the majority of the confirmed consumers will tell us that they began the use of the drug simply for "pleasure," if so it may be termed. The reason the Chinese choose opium may be because it is not so violent a stimulant as alcohol. The force of example and of fashion must also be taken into account in describing the reasons the Chinese have for taking opium. In society, restaurants and public places, opium is almost always offered.

2. *As a medicine.*—The second motive of the Chinese in using opium is due to the widespread popular belief in the medical efficacy of the drug. It has been proved in China that the opium habit, in the majority of cases, dates from the time when the drug was taken for medicinal purposes. In some cases the chronic or recurrent character of the malady necessitates repeated doses; in others the exhilaration and general sense of comfort induced, result in repetition long after the ailment for which the drug was originally taken has passed away. It is a common domestic medicine of the people. It is taken in cases of specific disorders, such as dysentery, rheumatism, tuberculosis, diabetes, and diarrhœa. In malarial and damp tracts there is a general faith in its virtue, either for

[1] Read at the Fourth Annual Meeting of the Philippine Medical Association, March 3, 1907.

warding off or in curing fever. The use of opium as a household remedy has a special importance in a country like China, where the mass of the population is beyond the reach of modern, qualified doctors. Although there are a large number of old-fashioned native practitioners, yet they are only to be found in towns and are chiefly resorted to by persons in easy circumstances; therefore, the poorer sections of the community and especially the agricultural classes, must prescribe for their own ailments. In the country it is used by persons as a restorative and stimulant after they have done hard work or have been much exposed to wet and cold. It is also employed to enable individuals to undergo fatigue on long journeys, and also, on occasions, when special exertion is required. In the large cities the people believe opium to have a special quality as an aphrodisiac.

Enough has now been said concerning the motives of the Chinese in using opium, but before I discuss diseases produced by the habitual use of the drug I wish to say a few words in regard to the modes in which it is consumed.

As a general rule, the commonest and in fact the oldest way, is by smoking. This is done by using a special preparation. This method is employed by the majority of the people, and is the manner in which they find pleasure. In this way the drug is offered to guests on all social occasions. The second, the next most common method is by eating opium. The crude material, the prepared extract, the dried leaves, or more rarely, the patent pills, are used for the purpose. The users either chew the preparation, as is the case with the dried leaves, or they swallow it either as the pills and as the extract, or as morphine. These methods are used by the poorer classes, because they are cheaper and more effective; that is they are generally used by persons who can not afford the luxury of smoking, or who have reached a condition in which smoking no larger satisfies their craving.

The method of hypodermic injection is also used, this is of course of more recent introduction, it is the most harmful and fortunately, the least used. Hydrochloride or sulphate of morphine are generally employed. Hypodermic injections are also habitual with a percentage of individuals of the poorer classes, because comparatively, they are the cheapest of all. Persons who no longer obtain the desired effect by smoking and eating, and those who originally contracted the habit after they first used opium as a medicine to stop pain; or those who desire to have a speedy action of the drug, also employ it. Some individuals have the habit of using all the methods mentioned, that is; smoking, eating and hypodermic injection.

RESULTS OF THE HABITUAL USE OF OPIUM AND THE DISEASES PRODUCED BY IT.

As a rule, confirmed opium consumers owing to the life they lead are predisposed to all varieties of acute or chronic diseases. The narcotic influences which affect the entire system, physically, morally and mentally, act as a sufficiently predisposing factor, but there are many diseases which I believe, are due to the direct action of the opium upon the individual system, although the drug can not be considered as a direct pathogenic cause.

The alimentary canal.—The immediate, specific and remote action of opium on the alimentary canal when the drug is taken per oram is well known. Habitual opium consumers always suffer from dyspepsia. Owing to the action of the drug on the intestines, its consumers are constipated. However, among chronic users of the drug when very large doses are employed, the splanchnic nerves are paralyzed in such degree that diarrhœa (called by the Chinese "opium diarrhœa)" results. This is regarded as a serious and fatal malady, as many persons succumb to it. Opium smokers are always anæmic, partially because the bronchial tubes are continually filled with smoke, with a resultant interference with perfect oxidation. They also suffer from a general, chronic catarrhal condition of the entire respiratory tract, due to the constant and direct irritating action of the smoke on the mucous membrane. The depressing effect of opium on the respiratory centers diminishes the movements of the chest. For these reasons opium users are predisposed to lung troubles and, to judge from my experience in practice, in the greater number of cases the cause of death among these persons is either tuberculosis of the lungs, bronchitis or not uncommonly hypostatic pneumonia, which is produced by the recumbent position which the consumers always assume. As a whole, without attempting to go into the details, I may say that nearly all the parts of the body are influenced by the use of opium. The brain is usually the chief organ affected, the subject is always drowsy, nervous, weak in character, wanting in energy, and utterly unfit for work. There is a general perversion of the mental faculties, self-control and judgment being weakened. When the craving is satisfied by using the drug, there is a brief period of excitement and exaltation which is generally described as a stimulation, but in reality I do not believe it to be so. In fact, this period consists rather in depression of the sensibility, by which the unfortunate person becomes unconcious of the miseries of his condition, and so accordingly he may be able to perform his duties, and to maintain his appearance better than when deprived of the poison. Melancholia and dementia are not infrequently seen among the habitués of the drug, as a

result of its prolonged and continuous use. The hepatic and general metabolism is greatly reduced in activity. Jaundice is often seen. Retention or incontinence of urine, and nocturnal emissions frequently occur. Persons who use hypodermic injections suffer from chronic abscesses appearing in the places where the needle punctures are found. Yawning, a prominent symptom of chronic opium poisoning, often leads to dislocation of the jaw.

Treatment of chronic opium poisoning.—Fully 25 per cent of the Chinese population of this city (6,000 individuals) are confirmed users of one or the other form of opium, and with the present law in effect, and the provision that on and after March 31, 1908, no opium will be imported except for medicinal purposes, our services in attending to the treatment of this chronic poisoning will become more and more necessary. It is true that the treatment of the chronic poisoning offers no very great hope if once a person has contracted the habit. However, in treating these cases it must be remembered that great variations in the intensity of the habit exist among various individuals, and one important point is to discover if the drug is being used as a medicine or for pleasure, for, as a rule, the latter condition is the more amenable to treatment.

There are three principal methods which we may, according to the condition of the patient, employ with fair success.

1. The sanitarium or retreat. 2. The gradual treatment. 3. The bromide or the alcohol treatment.

The first step is to induce the patient to resolve to break up the habit, the determination on the part of the patient himself being very important and absolutely necessary if successful results are to expected. Many cases are encountered in whom the self-control seems completely to have disappeared. However, if the contraction of the habit was due to pleasure and is only recent, determination on the part of the patient alone, together with a prescription of bitters by the physician, will often be sufficient to effect a cure. In these cases the patient is under the impression that the doctor is prescribing for him some medicine to take the place of opium, and he usually is satisfied with whatever he may be given. If restlessness on the part of the habitué is evident, then either the bromide or the alcohol treatment may be administered with fair success, but it must be remembered that bromide and alcohol are cardiac depressants and are to be given with caution, and from my experience, in not too large doses. Many have recommended 120 grains of bromide every two hours, until one ounce or more has been given to produce what is called the "bromide sleep." Others advise the administration of alcohol in such doses as to keep the patient under the influence of alcoholism for several days, when the further treatment is that for ordinary alcoholic excess. Both of these practices are, according to my opinion,

impractical and dangerous, as coma and death from syncope frequently occur. If bromide or alcohol is necessary at all, they must be given in small doses, as these remedies are applicable only when the patient has recently acquired the habit. In cases of long standing especially where the habit has been contrated because of an ailment, the immediate removal of the opium often leads to a recurrence of the former disease for which the drug was taken, or it produces such intense misery and depression as really to be dangerous. In such instance the gradual treatment, that is the slow cutting down of the amount consumed, would be more practical and safe. In very bad cases strict observation in an asylum or sanitarium is absolutely necessary.

The treatment of opium habit by such drugs as cocaine and heroine is worse than useless, because the patient merely breaks off one habit to contract another which may be worse.

EDITORIAL.

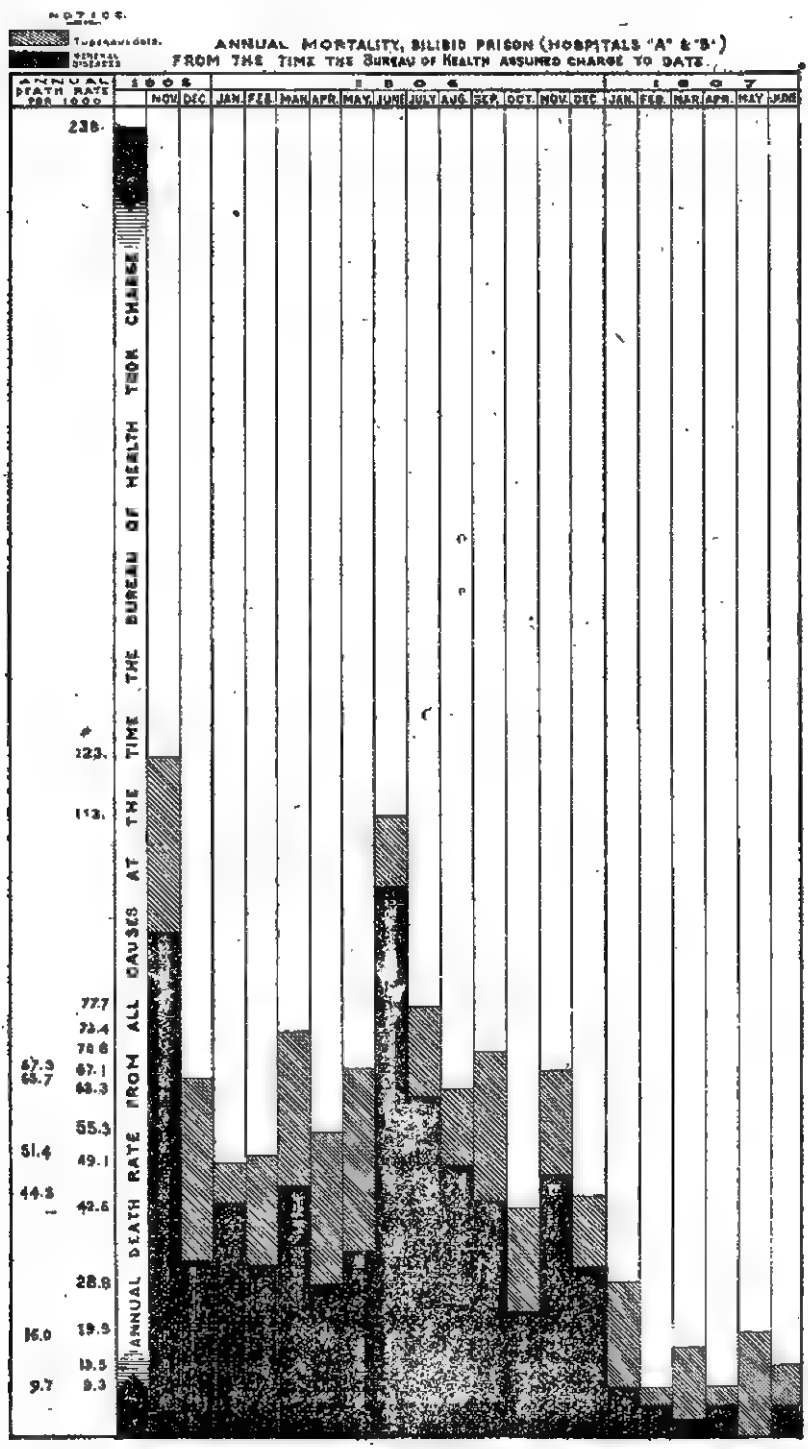
The sanitary and medical work in the Philippine Islands have developed to such an extent that beginning with the Medical Section of Volume III of this JOURNAL, it will be possible to introduce a series of editorials having direct connection, not only with laboratory investigation, but also with the statistical and other results of the medical advances in these Islands. Much material which has gradually accumulated, but which is not of such a nature as to be brought together in formal discussions of research is of the greatest interest to all who are concerned with scientific work in the tropics and it has seemed proper to afford a place in this JOURNAL for the publication of these results. It therefore will be the future policy of this JOURNAL to publish an editorial section of this character in each number of Section B.

PAUL C. FREER.

PROPHYLACTIC MEDICINE AS APPLIED TO THE HYGIENE OF BILIBID PRISON.

Probably one of the most satisfactory results that has ever been achieved by prophylactic medicine is that obtained by the Bureau of Health since the medical work of Bilibid Prison was placed under its charge in November, 1905. The diagram on the following page will show most effectively how the death rate has decreased from 238 per thousand to 13.5 per thousand at the end of June, 1907.

One of the first moves after taking charge was to improve the sanitary condition by admitting light and air and to relieve the overcrowding which was believed to be an important factor in the excessive mortality. A number of structural improvements were made; all the drains were deepened and made semicircular; the level of the ground was raised, and a system of daily sprinkling instituted. Drinking-water barrels were provided with locked covers to guard against contamination. Rigid inspections were made of all latrines. Prisoners who were ill were encouraged to come into the hospital upon the appearance of their first symptoms. Some months after the introduction of these immediate measures, the death rate was reduced to an average of about 75 per thousand, and here it remained; it seemed impossible to lower it further. Like everything else, there was a reason for this. The prisoners were


NOTICE.
Tuberculosis.
Venereal Diseases.
ANNUAL MORTALITY, BILIBID PRISON (HOSPITALS "A" & "B")
FROM THE TIME THE BUREAU OF HEALTH ASSUMED CHARGE TO DATE.
ANNUAL DEATH RATE PER 1000
1905
1906
1907
NOV. DEC. JAN. FEB. MAR. APR. MAY. JUNE JULY AUG. SEP. OCT. NOV. DEC. JAN. FEB. MAR. APR. MAY. JUNE
238.
223.
113.
77.7
73.4
78.6
67.9
68.7
67.1
68.3
55.3
51.4
49.1
44.8
42.6
28.8
16.0
19.5
13.5
9.7
8.3
ANNUAL DEATH RATE FROM ALL CAUSES AT THE TIME THE BUREAU OF HEALTH TOOK CHARGE

dying with ailments that should not have killed them; their powers of resistance were evidently impaired. The habits and customs of the people with reference to eating immediately suggested a clue and a remedy. The clue pointed to some extraordinary drain on the system. There was plenty of food, but imperfect nourishment. To discover the cause, a routine practice was inaugurated and the fæces of every prisoner in the prison were examined either by members of the staff of the Bureau of Science or by Dr. Shattuck, of the Bureau of Health, for the presence of ova of intestinal parasites; these were found to be present in about 60 per cent of all cases examined. Active therapeutic measures were inaugurated to rid the patients of the causes of these debilitating troubles and the result was immediately satisfactory; the death rate falling below 20 per thousand.

The prevailing diseases treated in Hospital A, Bilibid Prison, were agchylostoma, 1,537 cases; amœbic dysentery, 551 cases; acute dysentery, 174 cases; cholera, 18 cases; pneumonia, 62 cases; beriberi, 60 cases; conjunctivitis, 221 cases, and malaria, 174 cases.

During the previous year only 39 cases of agchylostoma were treated as compared with 1,537 cases during the present year. There have been 551 cases of amœbic dysentery treated as against 111 cases for the preceding year. These figures do not by any means indicate a greater prevalence of this disease and may be explained on the ground that the cases were detected by the systematic stool examinations which have been practiced. Among the rarer parasites that have been found are *Paragonimus westermanii*, 9 cases; *Schistosoma japonicum*, 15 cases: *Opisthorchis sinensis*, 5 cases; *Balantidium coli*, 14 cases; *Tænia saginata*, 20 cases; *Tænia solium*, 2 cases; and *Tænia nana*, 3 cases.

VICTOR G. HEISER.

INTESTINAL PARASITES IN THE PHILIPPINES.

The establishment of a separate department of medical zoölogy in the curriculum of the Philippine Islands Medical School is a step that has been taken to meet in a fundamental and comprehensive manner the seriousness and magnitude of the problem presented by the extreme prevalence of animal parasites among the Filipinos.

The publications of Strong, Musgrave, Shattuck, Cole, Smith, Ashburn, Craig and others have contributed information regarding the species of intestinal worms present in the Islands and the frequency with which certain forms had been encountered, and have served as a basis for the opinion generally prevalent that when the condition become actually known, the population of the Philippines would present one of the most striking instances in the history of medicine of almost universal infection with intestinal worms. With a view to obtaining accurate

information concerning the actual percentage of Filipinos infected with animal parasites, the Bureau of Science is at present tabulating the results of the examination of over 4,000 men from the different provinces. While the tabulation is not completed, it has been carried sufficiently far to indicate with fair certainty than not less than 80 per cent of the population of the Islands is infected with one or more species of intestinal worms and that if we consider the different species separately, there is an average of about 200 infections to each 100 of population.

The most comprehensive statistics regarding the prevalence of intestinal worms in tropical countries are those of Dobson and of Fearnside in India, and of the Porto Rican Anæmia Commission. The latter reported about 90 per cent of the population infected and the number of infections with all intestinal worms to be about 140 to each 100 of the population. Fearnside and Dobson each found about 100 infections to 100 people in India.

The relative frequency of different species in the Philippines is not yet definitely determined, further than that hookworms, *Ascaris* and *Trichuris*, are the most prevalent forms and that the first probably infect from 50 to 60 per cent of the total native population. In certain provinces, the ratio of hookworm infection is undoubtedly much higher.

One peculiarity presented by the situation is the fact that while this high proportion of the population shows hookworm infection, severe clinical manifestations of uncinariasis are comparatively rare. While hundreds of cases come annually from the provinces to the hospitals of Manila, exceedingly few, in the absence of malaria and other anæmia-producing diseases, present even mild anæmia, and the infection is discovered in the course of the usual routine stool examinations. Furthermore, careful inquiry among medical men of the Army, Navy, Bureau of Health, and Constabulary, who have served in the provinces, has failed to elicit reports of any remarkable prevalence of anæmia among the people.

Whether or not the explanation of this apparent rarity of clinical symptoms in hookworm infections among the Filipinos is a racial immunity on the part of the people to the toxins secreted by the worms, as has been suggested as the cause of a very similar rarity of symptoms found in negroes, by Stiles in the Southern States and by the Anæmia Commission in Porto Rico, the fact that severe clinical manifestations of uncinariasis are rare in the Philippines materially alters the problem which is presented. Instead of producing an acute condition demanding prompt and radical measures, such as were adopted in Porto Rico, St. Gothard's tunnel, the Westphalian coal mines, and other places where uncinariasis prevailed in its severer forms, it would appear that in the

Philippines hookworm infections play a part more nearly resembling that of the other common intestinal worms to which no definite pathology or severe symptomatology is usually attributed.

In other words, the population of the Philippines presents a higher percentage of infection with intestinal worms than has ever been definitely reported from any other people and the condition is essentially a chronic one, the results of which manifest themselves indirectly in the general physical impoverishment of the people and the high rate of morbidity and mortality accredited to other diseases.

In this connection it is interesting to mention the startling results apparently accomplished by the Bureau of Health, in coöperation with the Bureau of Science, at Bilibid Prison, where the original annual rate of mortality was reduced from about 238 per thousand to about 75 per thousand by the institution of general sanitary measures; then resisted further reduction until the prisoners began to be systematically treated for intestinal worms; after which, the death rate dropped to about 13 per thousand. Whether or not this apparent relationship between intestinal worms and the death rate at Bilibid will be substantiated by future records at the prison or by the institution of a similar campaign throughout the Islands, its significance can scarcely be overestimated even though ultimately the results should prove to be but a fraction of what was apparently accomplished among the Bilibid prisoners, and it sharply emphasizes the fact that the absence of direct, acute manifestations of intestinal helminthiasis should not blind us to the vital importance of this so nearly universal prevalence of intestinal worms as a factor in the present hygienic and industrial status of the Filipino people.

When we consider that there are about 6,000,000 inhabitants in the Islands and that, if present indications are verified, nearly 5,000,000 are infected with intestinal worms, and when we consider further the sanitary conditions which universally exist outside of the larger cities, the magnitude of the problem presents itself, and while we believe thoroughly in the local efficacy of the immediate institution of vigorous crusades by such means as are already at hand, it would seem perfectly apparent that any means which are to reach conditions in the mass of the population must aim at the education and training first of the native physicians and ultimately of the people themselves.

By giving medical zoölogy a prominent position in the course of instruction it is intended properly to emphasize the local importance of the subject which the above indications would seem to warrant, and it is the purpose of the school not only to train its native students in the diagnosis and treatment of parasitic diseases, but also to instruct them thoroughly in the life cycles of the parasites, modes of infection,

and methods of prophylaxis, in order that they may be sent out not only as general practitioners realizing the importance of treating infections with intestinal worms, but also to serve as sanitary officers in the towns, municipalities and provinces of the Islands, capable of intelligently enforcing sanitary regulations against animal parasites and of instructing the people concerning the reason and necessity of the measures enforced.

PHILIP E. GARRISON.

OCCURRENCE OF TUBERCULOSIS IN ONE HUNDRED AUTOPSIES IN THE PHILIPPINE ISLANDS.

In a consecutive series of necropsies at the Philippine Medical School, active tuberculosis was found in thirty-four of the first one hundred cases and was with its complications, the cause of death in all but two of the thirty-four.

The lungs were involved in thirty-three cases, the disease in the other being apparently confined to the peritoneum, careful search failing to reveal any tuberculous focus elsewhere in the body. The most frequent type of lesion in the lung was the chronic, ulcerative form of the disease which occurred in twenty-four of the cases. The amount of lung tissue involved in this type of the disease was in many instances remarkable. More or less involvement of all lobes of both lungs, with a minimum amount of air-containing alveoli was present in seven of the series; of both upper lobes in five; of all lobes of the right lung in one; of the entire left lung in two; of all lobes of both lungs except the right middle, in one; of all the left lung and right lower in one; of the left upper in two; of the right upper in one; of the right lower and left lower lobe respectively in one each.

The miliary type of tuberculosis was found in five cases, in two of which it was the only form of lesion present and of the remaining seven, four showed caseous nodules as the prevailing lesion; a gelatinous pneumonia occurred in two and a chronic fibroid in one case. In all of the thirty-three autopsis there were lesions of the pleuræ varying from localized adhesions to complete obliteration of one or both pleural cavities, with varied fibrinous and calcareous changes.

Renal tuberculosis occurred in four of the above cases, the left organ being involved in two, the right in one and both in one. In one instance of kidney involvement the right suprarenal was also tuberculous and in addition one other case of suprarenal tuberculosis was encountered involving both glands, with no involvement of the kidneys.

Twenty of the cases of pulmonary tuberculosis showed caseation of the bronchial glands; three, similar lesions of the mediastinal; five, of the mesenteric and three, of the retroperitoneal lymph glands.

Lesions of the intestinal tract occurred as follows in seven cases: Ulceration of the upper part of the jejenum, one case, one of the ulcers having perforated; of the ileum alone, one; of the colon alone, two cases; of both ileum and colon, two. A general tuberculosis of the peritoneum was found in seven cases, in but one of which was there involvement of the intestinal mucosa.

Of other organs involved, the spleen contained foci in two, the vertebræ in two, and the bladder in two cases.

Against the thirty-four cases of active tuberculosis, healed tuberculous lesions were found in but eight of the one hundred bodies.

PHILIP H. GILMAN.

PREVIOUS PUBLICATIONS OF THE BUREAU OF GOVERNMENT LABORATORIES—Concluded.

(Concluded from second page of cover.)

No. 32, 1905.—Biological Laboratory: I. Intestinal Hæmorrhage as a Fatal Complication in Amœbic Dysentery and Its Association with Liver Abscess. By Richard P. Strong, M. D. II. The Action of Various Chemical Substances upon Cultures of Amœbæ. By J. B. Thomas, M. D., Baguio, Benguet. *Biological and Serum Laboratories:* III. The Pathology of Intestinal Amœbiasis. By Paul G. Woolley, M. D., and W. E. Musgrave, M. D.

No. 33, 1905, Biological Laboratory.—Further Observations on Fibrin Thrombosis in the Glomerular and in Other Renal Vessels in Bubonic Plague. By Maximilian Herzog, M. D.

No. 34, 1905.—I. Birds from Mindoro and Small Adjacent Islands. II. Notes on Three Rare Luzon Birds. By Richard C. McGregor.

No. 35, 1905.—I. New or Noteworthy Philippine Plants, IV. II. Notes on Cuming's Philippine Plants in the Herbarium of the Bureau of Government Laboratories. III. Hackel, "Notes on Philippine Grasses." IV. Ridley, "Scitamineæ Philippinenses." V. Clarke, "Philippine Acanthaceæ." By Elmer D. Merrill, Botanist.

No. 36, 1905.—A Hand-List of the Birds of the Philippine Islands. By Richard C. McGregor and Dean C. Worcester.

The previous publications of the Bureau were given out as bulletins in serial number pertaining to the entire Bureau. These publications, if they are desired, can be obtained by applying to the librarian of the Bureau of Science, Manila, P. I., or to the Director of the Bureau of Science, Manila, P. I. Correspondents will confer a favor by returning to the Bureau any previous publications which they may have in duplicate, as a number of bulletins are now out of print.

LIST OF PREVIOUS PUBLICATIONS OF THE MINING BUREAU (NOW DIVISION OF MINES OF THE BUREAU OF SCIENCE).

1890.—Descripción física, geológica y minera en bosquejo de la Isla de Panay por D. Enrique Abella y Casariego, Inspector General de Minas del Archipiélago.

1890.—Memoria descriptiva de los manantiales minero-medicinales de la Isla de Luzon, estudiados por la comisión compuesta de los Señores D. José Centano, Ingeniero de Minas y Vocal Presidente, D. Anacleto del Rosario y Sales, Vocal Farmacéutico, y D. José de Vera y Gómez, Vocal Médico.

1893.—Estudio Descriptivo de algunas manantiales minerales de Filipinas ejecutado por la comisión formada por D. Enrique Abella y Casariego, Inspector General de Minas, D. José de Vera y Gómez, Médico, y D. Anacleto del Rosario y Sales, Farmacéutico; precidido de un prólogo escrito por el Excmo. Sr. D. Angel de Avilés, Director General de Administración Civil.

1893.—Terremotos experimentados en la Isla de Luzón durante los meses de Marzo y Abril de 1892, especialmente desastrosos en Pangasinán, Unión y Benguet. Estudio ejecutado por D. Enrique Abella y Casariego, Inspector General de Minas del Archipiélago.

1901.—The Coal Measures of the Philippines. Charles H. Burritt.

1902.—Abstract of the Mining Laws (in force in the Philippines, 1902). Charles H. Burritt.

1902, Bulletin No. 1.—Platinum and Associated Rare Metals in Placer Formations. H. D. McCaskey, B. S.

1903.—Report of the Chief of the Mining Bureau of the Philippine Islands. Charles H. Burritt.

1903, Bulletin No. 2.—Complete List of Spanish Mining Claims Recorded in the Mining Bureau. Charles H. Burritt.

1903, Bulletin No. 3.—Report on a Geological Reconnoissance of the Iron Region of Angat, Bulacan. H. D. McCaskey, B. S.

1904.—Fifth Annual Report of the Mining Bureau. H. D. McCaskey.

1905.—Sixth Annual Report of the Chief of the Mining Bureau. H. D. McCaskey.

1905, Bulletin No. 4.—A Preliminary Reconnoissance of the Mancayan-Suyoc Mineral Region, Lepanto, P. I. A. J. Eveland, Geologist.

1905, Bulletin No. 5.—The Coal Deposits of Batan Island. Warren D. Smith, B. S., M. A., Geologist.

LIST OF PREVIOUS PUBLICATIONS OF THE ETHNOLOGICAL SURVEY (NOW DIVISION OF ETHNOLOGY, BUREAU OF SCIENCE).

(For sale at Bureau of Printing.)

Vol. I.—The Bontoc Igorot, by Albert Ernest Jenks. Paper, ₱4.50; half Morocco, ₱7.

Vol. II, Part 1.—Negritos of Zambales, by William Allen Reed. Paper, ₱1.25; half Morocco ₱3.75.

Vol. II, Part 2 and Part 3.—The Nabaloi Dialect, by Otto Scheerer. The Bataks of Palawan, by Edward Y. Miller. (Bound also in one volume with Part 1, Negritos of Zambales.) Paper, ₱1.25; half Morocco, ₱3.75. Combined half Morocco, ₱5.

Vol. III.—Relaciones Agustinianas de las razas del Norte de Luzon, by Perez. Not listed by Bureau of Printing.

Vol. IV, Part 1.—Studies in Moro History, Law, and Religion, by Najeeb M. Saleeby. Paper, ₱0.75; half Morocco, ₱3.25.

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[1] The first four bulletins in the ornithological series were published by The Ethnological Survey under the title "Bulletins of the Philippine Museum." The other ornithological publications of the Government appeared as publications of the Bureau of Government Laboratories.

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